Jan Please

Access DB# 68910

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: S. Kumar Examiner #: 69594 Date: 6/17/02
Art Unit: 1621 Phone Number 308-4519 Serial Number: 09/529,319
Mail Box and Bldg/Room Location: CM1 7A07 Results Format Preferred (circle): PAPER DISK E-MAIL
TE 12

If more than one search is submitted, please prioritize searches in order of need.

****

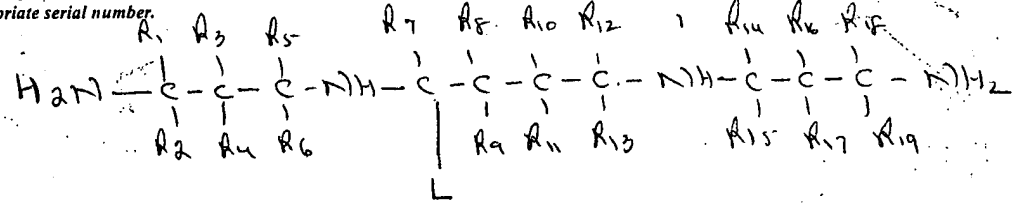
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

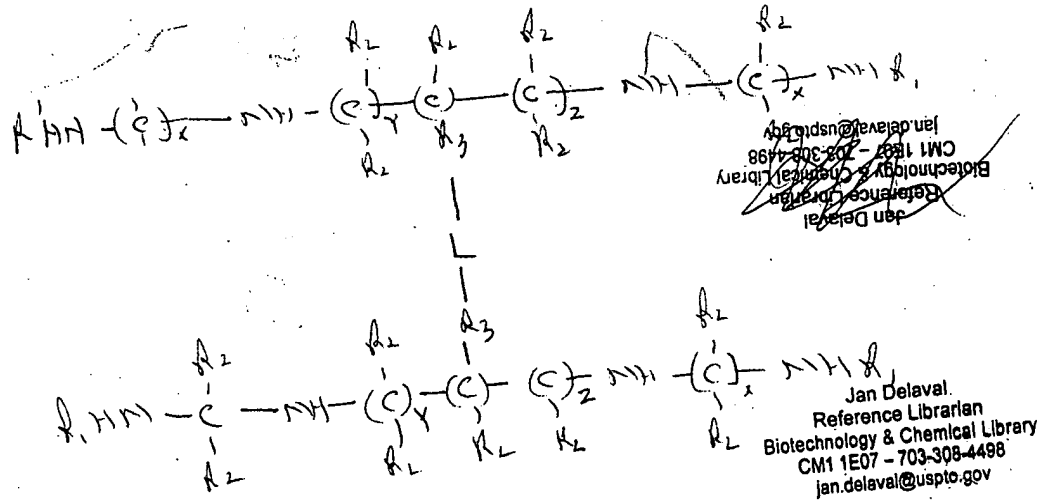
Title of Invention: Polyamine Transport Inhibitors.

Inventors (please provide full names): Richard Poulin et al

Earliest Priority Filing Date:

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

① 

② 

See claims 24, 32 34, 36, 38

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Searcher: Jan
Searcher Phone #: 4/498
Searcher Location:
Date Searcher Picked Up: 7/1/02
Date Completed: 7/1/02
Searcher Prep & Review Time:
Clerical Prep Time: 45
Online Time: < 90

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#) ✓
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

RECEIVED JUN 17 2002 BIO-TECH

PTO-1590 (8-01)

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Reference Librarian
Biotechnology & Chemical Library
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jan.delaval@uspto.gov

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FILE COVERS 1907 - 1 Jul 2002  VOL 137 ISS 1
FILE LAST UPDATED: 30 Jun 2002  (20020630/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
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information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> d all hitstr tot l119

L119 ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2002 ACS
AN   2000:401776  HCAPLUS
DN   133:38223
TI   Polyamine amide derivative transport
     inhibitors, their preparation, and their therapeutic and
     diagnostic use
IN   Poulin, Richard; Audette, Marie;
     Charest-Gaudrealt, Rene
PA   Universite Laval, Can.; Ilex Oncology, Inc.
SO   PCT Int. Appl., 111 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  C07C237-10
     ICS  C07C323-41; A61K031-16
CC   1-6 (Pharmacology)
     Section cross-reference(s): 9, 23, 63
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2000034226      A1   20000615       WO 1998-US26493  19981210 <--
         W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK,
             EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
             LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9919988         A1   20000626       AU 1999-19988    19981210 <--
PRAI WO 1998-US26493    A    19981210  <--
OS   MARPAT 133:38223
AB   The application discloses synthetic derivs. of original polyamines
```

in which a carbon atom to the original **polyamine** comprises an amide group **inhibits** the cellular uptake of a natural **polyamine** by specifically binding a cellular **transporter** for a natural **polyamine**. The synthetic derivs. are used to **inhibit** the activity of a natural **polyamine transporter** in the treatment of disorders involving unrestrained cell proliferation and/or differentiation where control of **polyamine transport** is required When used in combination with an **inhibitor** of **polyamine** synthesis.

ST **polyamine** amide deriv prepn **transport inhibition**; cell proliferation disorder **polyamine** amide deriv; differentiation cell disorder **polyamine** amide deriv

IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(diamines, **transport**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Antitumor agents
(mammary gland, ZR-75-1; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Mammary gland
(neoplasm, ZR-75-1, diamine and **polyamine transport** in; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Mammary gland
Mammary gland
(neoplasm, **inhibitors**, ZR-75-1; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Amide group
Cell differentiation
Cell proliferation
Cytotoxic agents
Diagnosis
Drug delivery systems
(**polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT **Biological transport**
(**polyamine transporter**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamines**, nonpolymeric; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Proliferation **inhibition**
(proliferation **inhibitors**; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT Structure-activity relationship
(**transport**-affecting; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

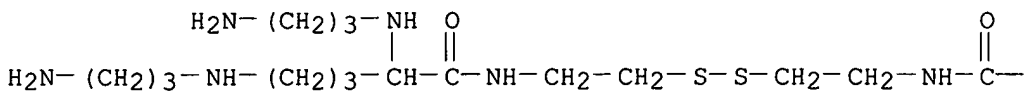
IT **Biological transport**
(uptake; **polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

IT 71-44-3, Spermine
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study);

PROC (Process)
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT 56-18-8, Norspermidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT **206760-63-6P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT **189076-31-1P** 206760-64-7P 206760-65-8P 206760-66-9P
247187-67-3P 247187-68-4P 275353-77-0P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT 70052-12-9, .alpha.-Difluoromethylornithine **206760-67-0**
206760-68-1 206760-69-2 206760-70-5
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT 110-60-1, Putrescine 124-20-9, Spermidine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
IT 119798-07-1P 186002-24-4P 206760-72-7P 213131-55-6P 244033-31-6P
275353-76-9P 275353-78-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; **polyamine** amide deriv.
transport inhibitor prepn. and diagnostic and
therapeutic use)
IT 56-17-7, Cystamine dihydrochloride 76-83-5, Trityl chloride 623-24-5
22834-83-9, Ornithine hydrochloride 24424-99-5, Di-tert-butyl dicarbonate 275353-75-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **polyamine** amide deriv. **transport**
inhibitor prepn. and diagnostic and therapeutic use)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Audette, M; WO 9817623 A 1998 HCAPLUS
(2) Hubert, M; Journal of Biological Chemistry 1996, V271(44), P27556
IT **206760-63-6P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor**
prepn. and diagnostic and therapeutic use)
RN 206760-63-6 HCAPLUS

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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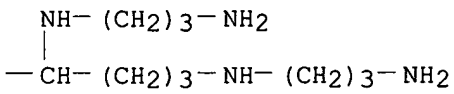
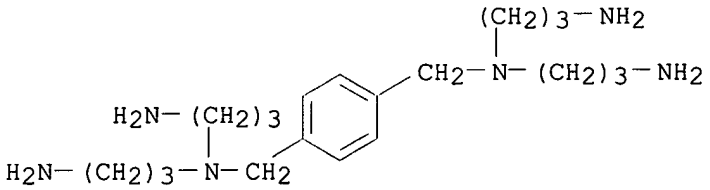
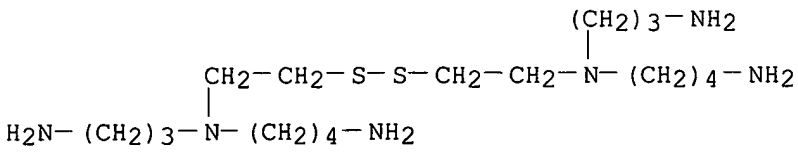


IT **189076-31-1P 247187-67-3P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

RN 189076-31-1 HCAPLUS
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)



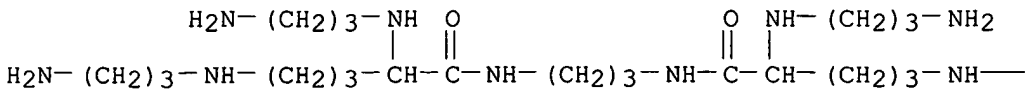
RN 247187-67-3 HCAPLUS
CN 1,4-Butanediamine, N,N''-(dithiodi-2,1-ethanediyl)bis[N-(3-aminopropyl)- (9CI) (CA INDEX NAME)



IT **206760-67-0 206760-68-1 206760-69-2 206760-70-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(**polyamine** amide deriv. **transport inhibitor** prepn. and diagnostic and therapeutic use)

RN 206760-67-0 HCAPLUS
CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

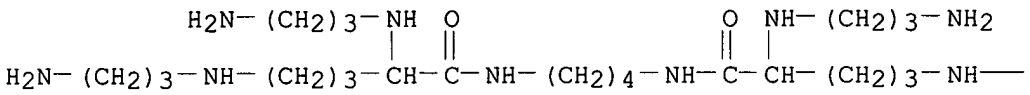


PAGE 1-B

—$(CH_2)_3$—NH_2

RN 206760-68-1 HCAPLUS
CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

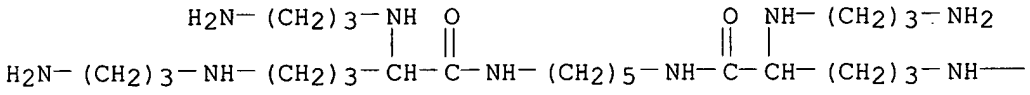


PAGE 1-B

—$(CH_2)_3$—NH_2

RN 206760-69-2 HCAPLUS
CN Pentanamide, N,N'-1,5-pentanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

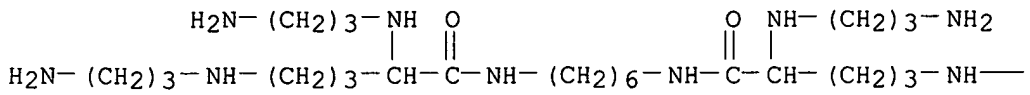


PAGE 1-B

—$(CH_2)_3$—NH_2

RN 206760-70-5 HCAPLUS
CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

L119 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:367983 HCAPLUS
DN 133:22412
TI Cationic lipids for use liposomes for drug delivery
IN Xiang, Gao
PA Vanderbilt University, USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N033-12
ICS A01N037-18; C07C225-00; C07C233-00; C07D265-30
CC **63-6** (Pharmaceuticals)
Section cross-reference(s): 3, 23
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000030444	A1	20000602	WO 1999-US27841	19991123 <--

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1998-109950P P 19981125 <--
US 1998-110970P P 19981204 <--
OS MARPAT 133:22412
AB The present invention relates to synthetic cationic lipids, liposome formulations and the use of such compds. to introduce functional bioactive agents into cultured cells.
ST liposome drug delivery cationic lipid
IT Gene therapy
Transformation, genetic
(cationic lipids for use liposomes for drug delivery)
IT Ionomers
Polyamides, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cationic lipids in liposomes for drug delivery)
IT Lipids, biological studies
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cationic; cationic lipids for use liposomes for drug delivery)
IT Drug delivery systems
(liposomes, cationic; cationic lipids for use liposomes for drug delivery)
IT **Polyamines**
Polyamines
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(polyamide-; cationic lipids in liposomes for drug delivery)

IT Polyamides, biological studies
Polyamides, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**polyamine**-; cationic lipids in liposomes for drug delivery)

IT 279674-76-9P 279674-81-6P 279675-37-5P 284491-03-8P 284491-49-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cationic lipids in liposomes for drug delivery)

IT 272462-70-1P 272462-71-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pren. and reactions of; cationic lipids for use liposomes for drug delivery)

IT 272462-76-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and reactions of; cationic lipids for use liposomes for drug delivery)

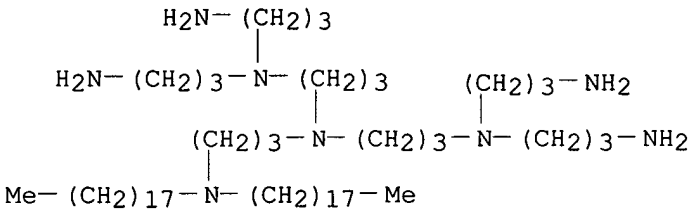
IT 272462-66-5P 272462-67-6P 272462-68-7P 272462-69-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reactions of; cationic lipids for use liposomes for drug delivery)

IT 272462-72-3 **272462-73-4**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of; cationic lipids for use liposomes for drug delivery)

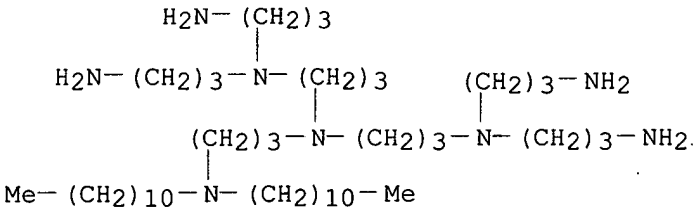
IT 57-88-5DP, Cholesterol, conjugates with polyethyleneimine 13055-09-9P 15337-57-2P 89101-38-2P 117458-00-1P 134925-48-7P 179075-30-0P 179075-31-1P 197974-80-4P 200182-20-3P 209396-83-8P 272462-77-8P 272462-79-0P 272462-80-3P 272462-81-4P 272462-82-5P 272462-83-6P 272462-84-7P 272462-85-8P 272462-86-9P 272462-87-0P 272462-88-1P 272462-89-2P 272462-90-5P 272462-91-6P 272462-92-7P 272462-93-8P 272462-94-9P 272462-95-0P 272462-96-1P 272462-97-2P 272462-98-3P 272462-99-4P 272463-00-0P 272463-01-1P 272463-02-2P 272463-03-3P 272463-04-4P 272463-05-5P 272463-06-6P 272463-07-7P 272463-08-8P 272463-09-9P 272463-10-2P 272463-11-3P 272463-12-4P 272463-13-5P 272463-14-6P 272463-15-7P 272463-16-8P 272463-17-9P 272463-18-0P 272463-19-1P 272463-20-4P 272463-21-5P 272463-22-6P 272463-23-7P 272463-24-8P 272463-25-9P 272463-26-0P 272463-27-1P 272463-28-2P 272463-29-3P 272463-30-6P 272463-31-7P 272463-32-8P 272463-33-9P 272463-34-0P 272463-35-1P 272463-36-2P 272463-37-3P **272463-38-4P** 272463-39-5P 272463-40-8P 272463-41-9P 272463-42-0P 272463-43-1P 272463-44-2P 272463-45-3P 272463-46-4P 272463-47-5P 272463-48-6P 272463-49-7P 272463-50-0P 272463-51-1P 272463-52-2P 272463-53-3P 272463-54-4P 272463-55-5P 272463-56-6P 272463-57-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of; cationic lipids for use liposomes for drug delivery)

IT 98-88-4, Benzoyl chloride 102-71-6, reactions 107-13-1, 2-Propenenitrile, reactions 110-91-8, Morpholine, reactions 112-77-6, Oleic acid chloride 112-99-2, Dioctadecylamine 123-46-6 540-51-2, 2-Bromoethanol 566-88-1, 5.alpha.-Cholestan-3-one 598-21-0, Bromoacetylbromide 616-30-8, (.+-.)-3-Amino-1,2-propanediol 623-57-4 2442-61-7, 1,2-Dioleoylglycerol 3464-50-4, Cholesteryl chloroacetate 6110-53-8, Oleyl bromide 6425-32-7 13242-44-9, 2-Dimethylaminoethanethiol hydrochloride 15337-59-4 30189-36-7 30734-81-7 35709-09-2, Oleyl mesylate 272462-74-5 272462-75-6 272462-78-9
RL: RCT (Reactant); RACT (Reactant or reagent)

(reactions of; cationic lipids for use liposomes for drug delivery)
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Lerouge; Chem Phys Lipids 1988
IT **272462-73-4**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of; cationic lipids for use liposomes for drug delivery)
RN 272462-73-4 HCAPLUS
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(dioctadecylamino)propyl]- (9CI) (CA INDEX NAME)



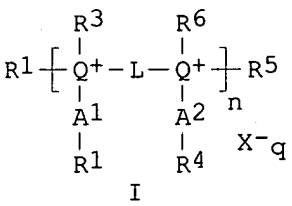
IT **272463-38-4P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of; cationic lipids for use liposomes for drug delivery)
RN 272463-38-4 HCAPLUS
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(diundecylamino)propyl]- (9CI) (CA INDEX NAME)



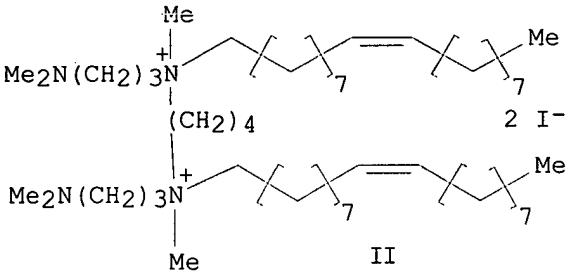
L119 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:335366 HCAPLUS
DN 132:334312
TI synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells
IN Chu, Yongliang; Masoud, Malek; Gebeyehu, Gulilat
PA Life Technologies, Inc., USA
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C211-64
ICS C07C211-63; C07C229-26; C07C211-21; A61K031-14
CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 3, 35, **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2000027795 A1 20000518 WO 1999-US26825 19991112 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1129064 A1 20010905 EP 1999-971794 19991112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI US 1998-108117P P 19981112 <--
WO 1999-US26825 W 19991112
OS MARPAT 132:334312
GI



I



II

AB Synthesis and activity of transfection reagents (I) [Q = N, O, S; L = (un)substituted alkyl, ether, polyether, amide, polyamide, ester, sulfide, urea, thiourea, guanidyl, carbamoyl, carbonate, phosphate, sulfate, sulfoxide, imine, carbonyl, secondary amine; R1-R6 independently = (un)substituted alkyl, alkenyl, aryl, ether; A1, A2 independently = CH2O, CH2S, CH2NH, CO, C=NH, CS, alkyl; X = physiol. acceptable anion; n = 1-1000; q = no. of pos. charge divided by valence of anion], cationic lipids capable of facilitating **transport** of biol. active agents or substances into cells, are disclosed. Thus, I [R1,R4 = oleyl; R2,R5 = Me2N(CH2)3; R3,R6 = Me; A1,A2 = CH2; L = (CH2)4; X = I] (II) is prepd. by reaction of bis-1,4-oleyl-1,4-butandiamine with acrylonitrile followed by redn. of nitrile to amine and quaternization of amine with Me iodide. II shows an activity of 37.8 ng/.beta.gal/cm2 in DNA delivery. Formulations contg. I are given.

ST cationic lipid prepn transfection reagent; DNA delivery gene therapy

IT Lipids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polar, cationic; synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)

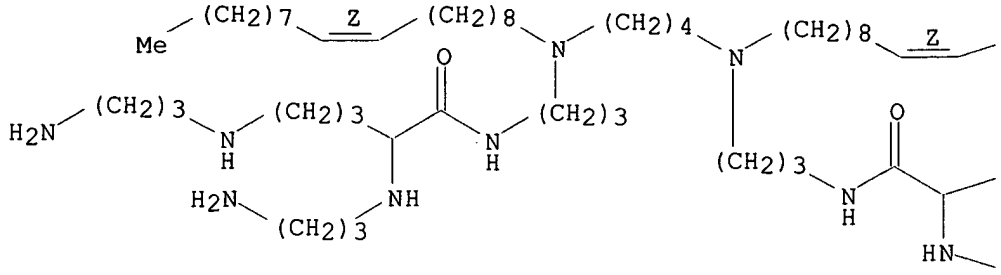
IT Gene therapy
Transformation, genetic
(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)

IT DNA
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(synthesis and activity of transfection reagents for **transport**

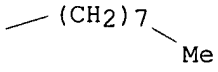
of biol. active agents or substances into cells)
IT 268539-52-2P **268539-53-3P 268539-54-4P** 268539-55-5P
268539-56-6P 268539-57-7P **268539-58-8P** 268539-59-9P
268539-60-2P 268539-61-3P 268539-62-4P 268539-63-5P
268554-12-7P 268554-14-9P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)
IT 50-99-7, Glucose, reactions 57-48-7, D-Fructose, reactions 57-50-1, reactions 59-23-4, Galactose, reactions 63-42-3, Lactose 69-79-4, Maltose 107-13-1, 2-Propenenitrile, reactions 110-60-1, 1,4-Diaminobutane 112-77-6, Oleoyl chloride 528-50-7, Cellobiose 3458-28-4, Mannose 4023-02-3 5455-98-1 213131-55-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)
IT 268539-45-3P 268539-46-4P 268539-47-5P 268539-48-6P 268539-49-7P 268539-50-0P 268539-51-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Can; WO 9840499 A 1998 HCAPLUS
(2) Gebeyehu, G; US 5334761 A 1994 HCAPLUS
(3) Genzyme Corporation; WO 9802190 A 1998 HCAPLUS
(4) Haces, A; US 5674908 A 1997 HCAPLUS
(5) Haces, A; WO 9742819 A 1997 HCAPLUS
(6) Henkel Und Cie G M B H; FR 1567214 A 1969 HCAPLUS
(7) La Roche, H; EP 0846680 A 1998 HCAPLUS
(8) Life Technologies Inc; WO 9840502 A 1998 HCAPLUS
(9) McCluskie, M; ANTISENSE NUCLEIC ACID DRUG DEV 1998, V8(5), P401 HCAPLUS
(10) McCluskie, M; Direct gene transfer to the respiratory tract of mice with pure plasmid and lipid-formulated DNA 1999, V130(8) HCAPLUS
(11) Shen, D; US 5830430 A 1998 HCAPLUS
(12) Smithkline Beecham Plc; WO 9929712 A 1999 HCAPLUS
(13) Wolff, J; US 5744335 A 1998 HCAPLUS
IT **268539-53-3P 268539-54-4P 268539-58-8P 268554-12-7P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(synthesis and activity of transfection reagents for **transport** of biol. active agents or substances into cells)
RN 268539-53-3 HCAPLUS
CN Pentanamide, N,N'-[1,4-butanediylbis[[(9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

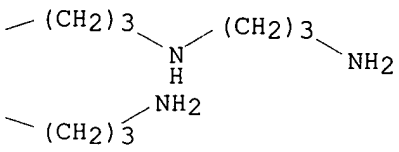
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

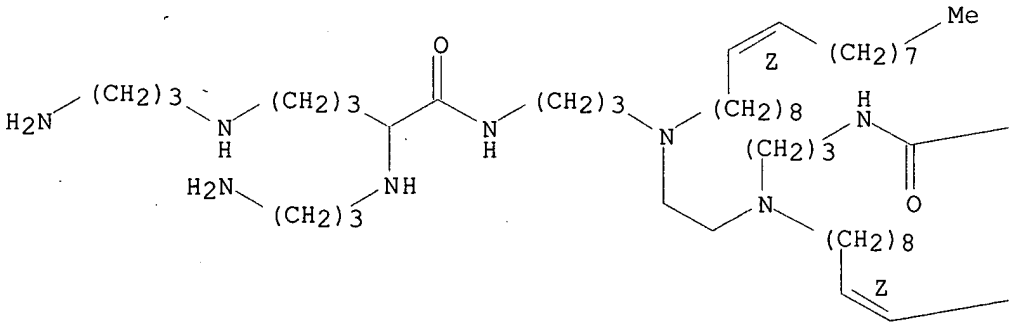




RN 268539-54-4 HCAPLUS
CN Pentanamide, N,N'-[1,2-ethanediylbis[[(9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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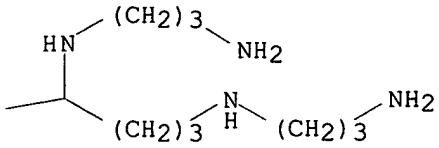
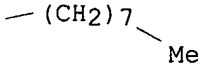
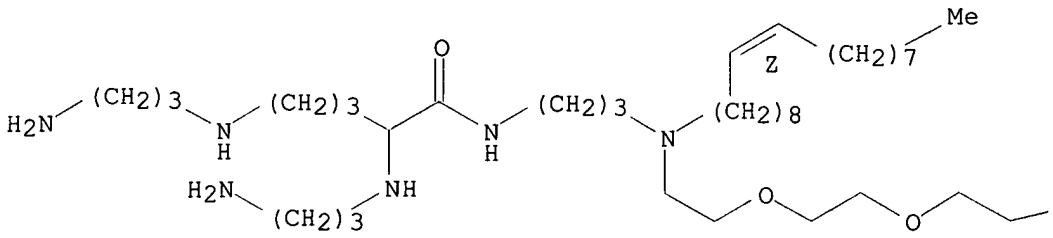




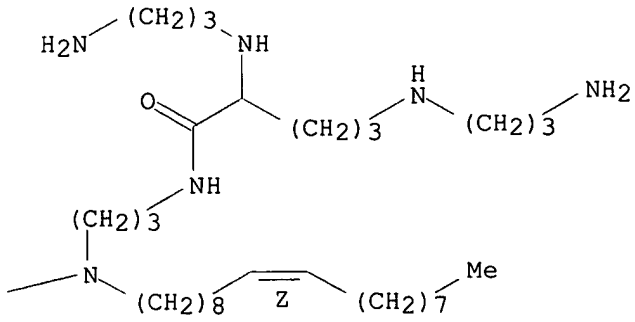
RN 268539-58-8 HCAPLUS
CN Pentanamide, N,N'-[4,13-di-(9Z)-9-octadecenyl-7,10-dioxa-4,13-diazahexadecane-1,16-diyl]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



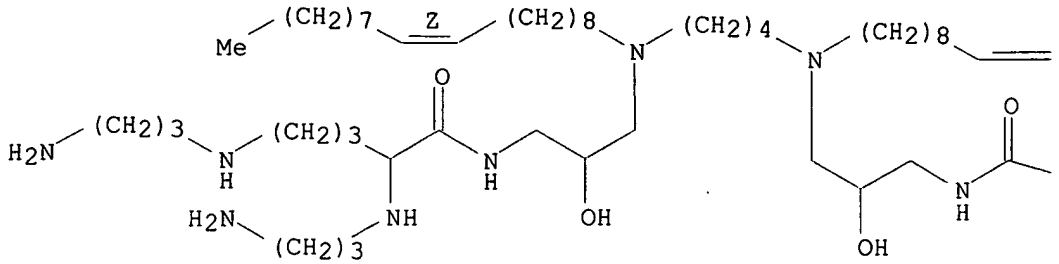
PAGE 1-B



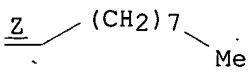
RN 268554-12-7 HCAPLUS
CN Pentanamide, N,N'-[1,4-butanediylbis[[(9Z)-9-octadecenylimino](2-hydroxy-3,1-propanediyl)]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

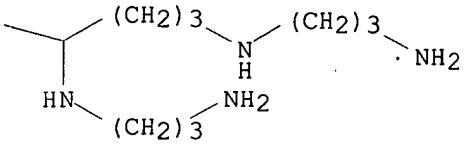
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B





L119 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:78926 HCAPLUS
DN 132:122935
TI Preparation of amide-based cationic lipids
IN Schwartz, David Aaron; Daily, William J.; Dwyer, Brian Patrick; Srinivasan, Kumar; Brown, Bob Dale
PA Genta, Incorporated, USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07C233-05
NCL 564153000
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 3, **63**
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6020526	A	20000201	US 1996-681297	19960722 <--
US 6339173	B1	20020115	US 1999-327392	19990607 <--
PRAI US 1996-681297	A1	19960722 <--		

AB Amide-based cationic lipids R2(NHCHR4CO)n(NHCHR3)pYCOR1 [X-]m (Y = bond, alkylene; R1 = H, lipophilic moiety; R2, R3, R4 = pos. charged moiety or H, alkyl, heterocyclyl; n, p = 0-8; X- = anion or polyanion; m = integer from zero to a no. equiv. to the pos. charge present on the lipid) or their salts, solvates , or enantiomers were prepd. The present invention further provides compns. of these lipids with polyanionic macromols., methods for interfering with protein expression in a cell utilizing these compns. and a kit for prepg. the same. Thus, N2-[N2,N5-bis(3-aminopropyl)-L-ornithyl]-N,N-dioctadecyl-L-glutamine tetrahydrochloride (I) was prepd. via coupling of N2,N5-bis[(1,1-dimethylethoxy)carbonyl]-N2,N5-bis[3-[(1,1-dimethylethoxy)carbonyl]aminopropyl]-L-ornithine N-hydroxysuccinimidyl ester with N,N-dioctadecyl-L-glutamine benzyl ester hydrotrifluoroacetate,

followed by hydrogenolysis over Pd/C and deprotection using HCl in dioxane. The synthesized cationic lipids, including I, were assayed for transient transfection efficiency in COS-7, SNB-19, RD and C8161 cells and for nuclear delivery of oligonucleotides of varying charge densities.

ST peptide amide cationic lipid prepn transfection

IT Transformation, genetic
(prepn. of amide-based cationic lipids)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amide-based cationic lipids)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of amide-based cationic lipids)

IT 176021-45-7P 187978-83-2P 187978-84-3P 187978-86-5P 187978-87-6P
187978-96-7P 187979-12-0P 187979-13-1P 187979-20-0P 187979-21-1P
187979-29-9P 187979-37-9P 187979-38-0P 187979-39-1P 187979-40-4P
219304-01-5P 256429-41-1P 256429-42-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amide-based cationic lipids)

IT 112-99-2P, Dioctadecylamine 504-53-0P, Stearone 556-50-3P,
Glycylglycine 1947-00-8P 2566-19-0P 6136-90-9P, 18-
Pentatriacontanone, oxime 7536-58-5P 13574-13-5P 30924-93-7P
36243-55-7P, 18-Pentatriacontanamine 119798-08-2P 124050-79-9P
159684-91-0P 187978-89-8P 187978-90-1P 187978-92-3P 187978-93-4P
187978-97-8P 187979-00-6P 187979-02-8P 187979-03-9P 187979-04-0P
187979-06-2P 187979-08-4P 187979-10-8P 187979-15-3P 187979-17-5P
187979-18-6P 187979-19-7P 187979-22-2P 187979-23-3P 187979-25-5P
187979-26-6P 187979-27-7P 187979-30-2P 187979-32-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amide-based cationic lipids)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

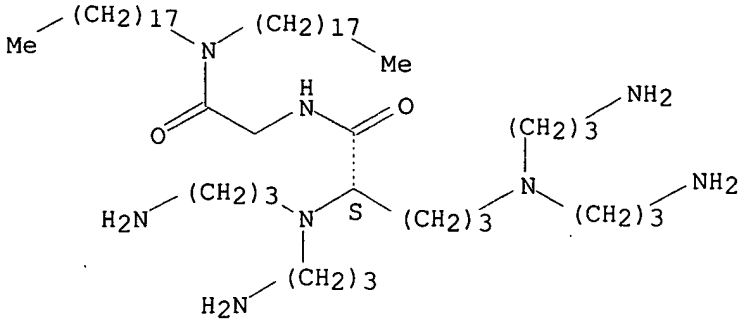
(1) Anon; WO 9601841 1996 HCAPLUS
(2) Beher; US 5171678 1992 HCAPLUS
(3) Eelgner; US 5264618 1993 HCAPLUS
(4) Eppstein; US 4897355 1990
(5) Felgner; Proc Natl Acad Sci USA 1987, V84, P7413 HCAPLUS
(6) Gebeyehu; US 5334761 1994 HCAPLUS
(7) Remy; Bioconjugate chem 1994, V5, P647 HCAPLUS

IT **219304-01-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amide-based cationic lipids)

RN 219304-01-5 HCAPLUS

CN Glycinamide, N2,N2,N5,N5-tetrakis(3-aminopropyl)-L-ornithyl-N,N-dioctadecyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L119 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:691066 HCAPLUS
DN 131:307091
TI **Polyamine transport inhibitors**, their preparation, and their therapeutic use
IN **Poulin, Richard; Audette, Marie; Charest-Gaudrealt, Rene**
PA Universite Laval, Can.; Ilex Oncology, Inc.
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C237-10
ICS C07C211-14; C07C323-41; A61K031-16; A61K031-13
CC 1-6 (Pharmacology)
Section cross-reference(s): 23, **63**
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9954283	A1	19991028	WO 1998-US7806	19980421 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2304557	AA	19991028	CA 1998-2304557	19980421 <--
	AU 9871316	A1	19991108	AU 1998-71316	19980421 <--
	EP 1003715	A1	20000531	EP 1998-918385	19980421 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI WO 1998-US7806 A 19980421 <--
OS MARPAT 131:307091
AB The invention describes the design, synthesis and therapeutic use of a variety of novel **inhibitors** of **polyamine transport**. The main feature of this class of **transport inhibitors** is to incorporate a linker or side chain that prevents the uptake of **polyamines** and helps to conjugate **polyamine** analogs to form dimers with high **inhibitory** potency against **polyamine** uptake. These new compds. incorporate features that are designed to maximize their chem. and metabolic stability and their ability to bind to the **polyamine transporter**, and to minimize their toxicity by preventing their absorption by the cells. The purpose of such **inhibitors** is to prevent the uptake or salvaging of circulating **polyamines** by rapidly proliferating cells such as tumor cells, in order to potentiate the effect of

therapeutic **inhibitors** of **polyamine** biosynthesis such as .alpha.-difluoromethylornithene.

ST **polyamine transport inhibitor** prepn
therapeutic; antitumor **polyamine transport inhibitor** prepn

IT Affinity labeling
(affinity ligands; **polyamine transport inhibitor** prepn. and therapeutic use)

IT Antitumor agents
(mammary gland, ZR-75-1; **polyamine transport inhibitor** prepn. and therapeutic use)

IT Mammary gland
(neoplasm, ZR-75-1; **polyamine transport inhibitor** prepn. and therapeutic use)

IT Mammary gland
Mammary gland
(neoplasm, **inhibitors**, ZR-75-1; **polyamine transport inhibitor** prepn. and therapeutic use)

IT **Biological transport**
Cell differentiation
Cytotoxic agents
Diagnosis
Drug delivery systems
Drug interactions
(**polyamine transport inhibitor** prepn. and therapeutic use)

IT Metabolism
(**polyamine; polyamine transport inhibitor** prepn. and therapeutic use)

IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamines**, nonpolymeric; **polyamine transport inhibitor** prepn. and therapeutic use)

IT Proliferation **inhibition**
(proliferation **inhibitors; polyamine transport inhibitor** prepn. and therapeutic use)

IT Structure-activity relationship
(spermine **transport-inhibitory; polyamine transport inhibitor** prepn. and therapeutic use)

IT **Biological transport**
(uptake; **polyamine transport inhibitor** prepn. and therapeutic use)

IT 79-17-4, Aminoguanidine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**polyamine transport inhibitor** prepn. and therapeutic use)

IT **184895-97-4P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(**polyamine transport inhibitor** prepn. and therapeutic use)

IT 184895-98-5P 184895-99-6P 184896-08-0P **189076-31-1P** **247187-66-2P** **247187-67-3P** 247187-68-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(**polyamine transport inhibitor** prepn. and

therapeutic use)

IT 71-44-3D, Spermine, derivs. 110-60-1D, Putrescine, derivs. 124-20-9D, Spermidine, derivs. 70052-12-9, .alpha.-Difluoromethylornithine 184896-00-2 184896-01-3 184896-02-4 **206760-70-5** **247187-63-9 247187-64-0 247187-65-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(**polyamine transport inhibitor** prepn. and therapeutic use)

IT 71-44-3, Spermine 110-60-1, 1,4-Butanediamine 124-20-9, Spermidine 9001-53-0, Copper amine oxidase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamine transport inhibitor** prepn. and therapeutic use)

IT 119798-07-1P 119798-08-2P 124076-28-4P 184896-06-8P 184896-07-9P 244033-31-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; **polyamine transport inhibitor** prepn. and therapeutic use)

IT 56-17-7, Cystamine dihydrochloride 56-18-8, Norspermidine 70-26-8, Ornithine 76-83-5, Trityl chloride 107-13-1, 2-Propenenitrile, reactions 623-24-5, .alpha.,.alpha.'-Dibromo-p-xylene 24424-99-5, Di-tert-butyl dicarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **polyamine transport inhibitor** prepn. and therapeutic use)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Ask, A; Cancer Letters 1993, V69, P33 HCAPLUS
(2) Audette, M; WO 9817623 A 1998 HCAPLUS
(3) Aziz, K; Journal of Pharmacology and Experimental Therapeutics 1995, V274(1), P181
(4) Aziz, S; US 5456908 A 1995 HCAPLUS
(5) Hubert, M; Journal of Biological Chemistry 1996, V271(44), P27556
(6) Univ New York; WO 9312777 A 1993 HCAPLUS

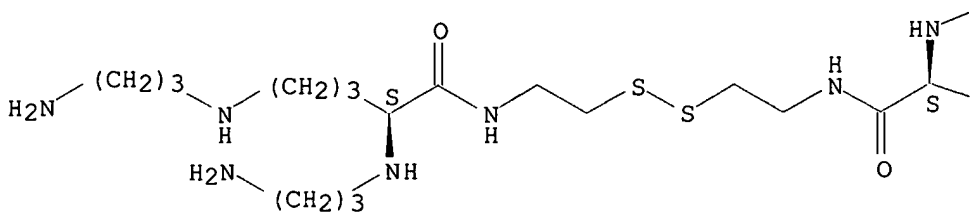
IT **184895-97-4P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(**polyamine transport inhibitor** prepn. and therapeutic use)

RN 184895-97-4 HCAPLUS

CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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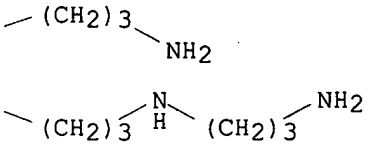
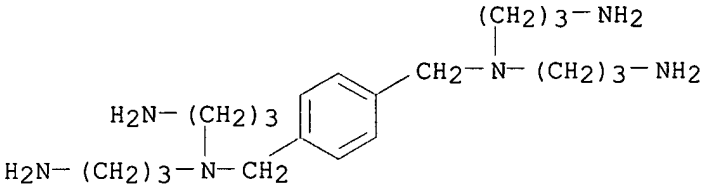


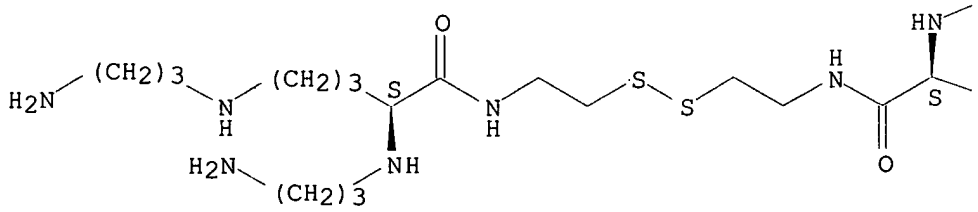
IT **189076-31-1P 247187-66-2P 247187-67-3P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(polyamine transport inhibitor prepn. and therapeutic use)
RN 189076-31-1 HCAPLUS
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)



RN 247187-66-2 HCAPLUS
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, octahydrochloride, (2S,2'S)- (9CI) (CA INDEX NAME)

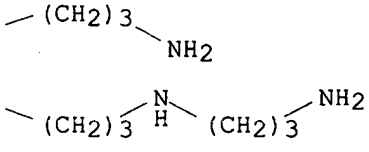
Absolute stereochemistry.

PAGE 1-A

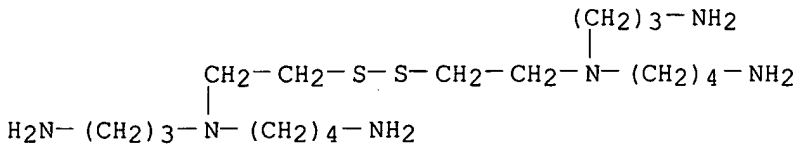


●8 HCl

PAGE 1-B

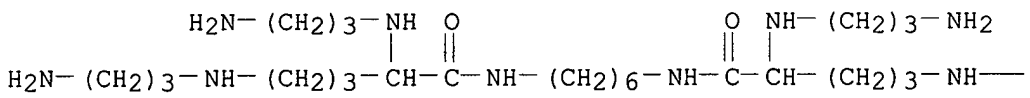


RN 247187-67-3 HCAPLUS
CN 1,4-Butanediamine, N,N''-(dithiodi-2,1-ethanediyl)bis[N-(3-aminopropyl)-(9CI) (CA INDEX NAME)



IT **206760-70-5 247187-63-9 247187-64-0**
247187-65-1
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(**polyamine transport inhibitor** prepn. and therapeutic use)
RN 206760-70-5 HCAPLUS
CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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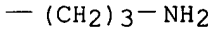
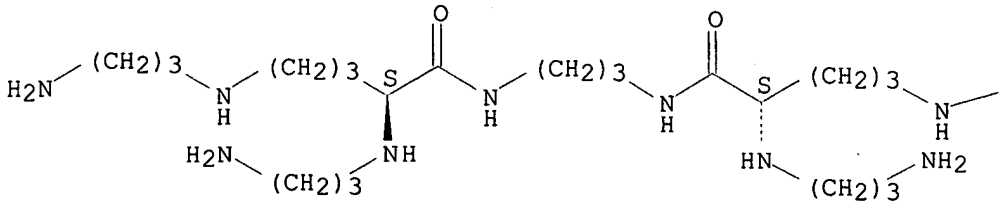


RN 247187-63-9 HCAPLUS
CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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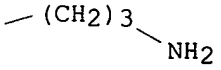
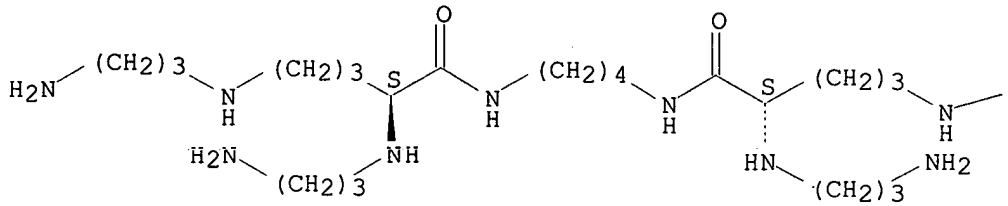


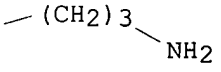
RN 247187-64-0 HCAPLUS
CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



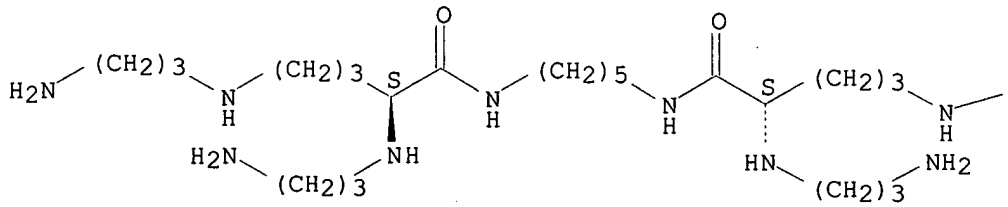
PAGE 1-B



RN 247187-65-1 HCAPLUS
CN Pentanamide, N,N'-1,5-pentanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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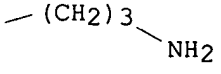

L119 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:404110 HCAPLUS
DN 131:228866
TI Synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**
AU Covassin, Laurence; Desjardins, Michel; **Charest-Gaudreault, Rene**; **Audette, Marie**; Bonneau, Marie-Josee; **Poulin, Richard**
CS Faculty of Pharmacy, Laval University, QC, G1K 7P4, Can.
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(12), 1709-1714
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 31-6 (Alkaloids)
Section cross-reference(s): 1
AB A series of novel spermidine and sym-norspermidine dimers was synthesized by crosslinking the polyamine backbones via alkylation of their secondary amino groups to Bu, trans-2-butenyl, 2-butynyl or p-xylyl bridges. The resulting hexamines behaved as high-affinity antagonists of polyamine uptake, with a relative potency that was dependent on the geometry of the linker structure.
ST spermidine dimer prepn polyamine **transport inhibitor**; norspermidine dimer prepn polyamine **transport inhibitor**
IT Structure-activity relationship
(antitumor; synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
IT Amines, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(polyamines, nonpolymeric; synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
IT Antitumor agents
Biological **transport**
(synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
IT **101394-77-8P 201859-92-9P 244033-18-9P 244033-19-0P 244033-20-3P 244033-21-4P 244033-22-5P 244033-23-6P 244033-24-7P 244033-25-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
IT 56-18-8, sym-Norspermidine 110-57-6 124-20-9, Spermidine 543-20-4, Succinyl chloride 623-24-5 821-10-3, 1,4-Dichloro-2-butyne
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
IT 163883-05-4P 244033-13-4P 244033-14-5P 244033-15-6P 244033-16-7P 244033-17-8P 244033-26-9P 244033-27-0P 244033-28-1P 244033-29-2P 244033-30-5P 244033-31-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Behr, J; Bioconjugate Chem 1994, V5, P382 HCAPLUS
(3) Bergeron, R; Bioinorg Chem 1986, V14, P345 HCAPLUS
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(7) Covassin, L; Unpublished results
(8) Demontigny, D; Unpublished results
(9) Duranton, B; Cancer Res 1997, V57, P573 HCAPLUS
(10) Huber, M; J Biol Chem 1996, V271, P27556 HCAPLUS
(11) Lessard, M; J Biol Chem 1995, V270, P1685 HCAPLUS
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(16) Seiler, N; Cancer Res 1990, V50, P5077 HCAPLUS
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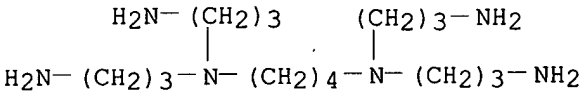
(18) Simard, J; Endocrinology 1990, V126, P3223 HCAPLUS
(19) Zang, E; Synth Commun 1997, V27, P3145 HCAPLUS

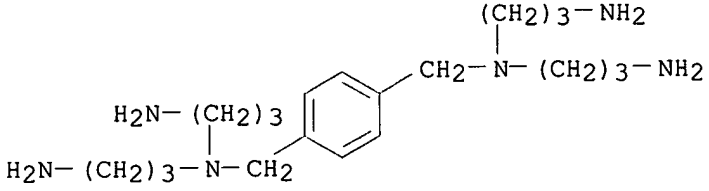
IT **101394-77-8P 201859-92-9P 244033-18-9P**
244033-19-0P 244033-20-3P 244033-21-4P
244033-22-5P 244033-23-6P 244033-24-7P
244033-25-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of spermidine and norspermidine dimers as high affinity polyamine **transport inhibitors**)

RN 101394-77-8 HCAPLUS
CN 1,4-Butanediamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



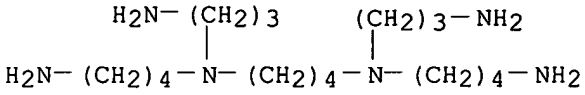
●6 HCl

RN 201859-92-9 HCAPLUS
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



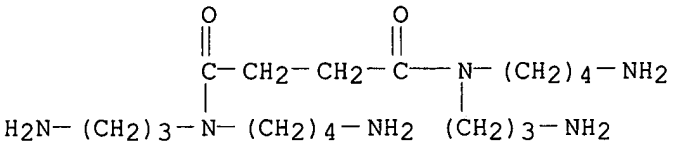
●6 HCl

RN 244033-18-9 HCAPLUS
CN 1,4-Butanediamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



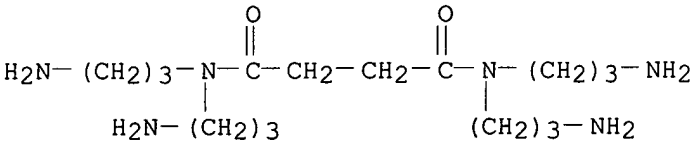
●6 HCl

RN 244033-19-0 HCAPLUS
CN Butanediamide, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

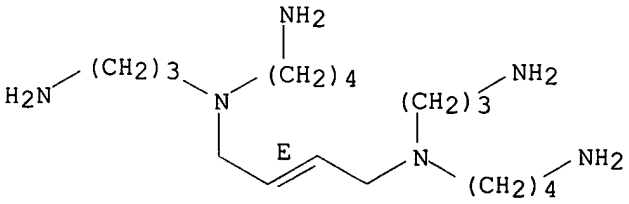
RN 244033-20-3 HCAPLUS
CN Butanediamide, N,N,N',N'-tetrakis(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

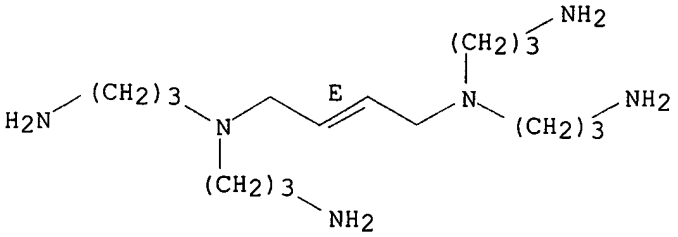
RN 244033-21-4 HCAPLUS
CN 2-Butene-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

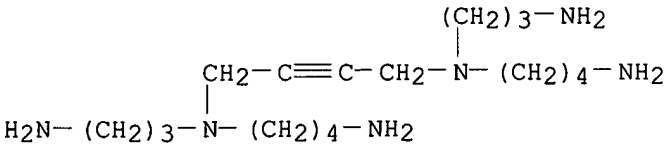


RN 244033-22-5 HCAPLUS
CN 2-Butene-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)

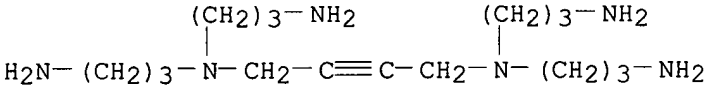
Double bond geometry as shown.



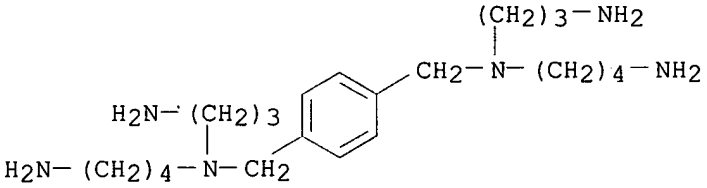
RN 244033-23-6 HCAPLUS
CN 2-Butyne-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)



RN 244033-24-7 HCAPLUS
CN 2-Butyne-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)



RN 244033-25-8 HCAPLUS
CN 1,4-Benzenedimethanamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)



● 6 HCl

L119 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:136874 HCAPLUS
DN 130:153974
TI Preparation of novel lipopolyamines and their use in **transport** liposomes for carrying transfection agents
IN Klosel, Roland; Konig, Stephan
PA Biontex Laboratories G.m.b.H., Germany
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA German

IC ICM C07C211-14
ICS C07C237-10; A61K047-18
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, **63**
FAN.CNT 1

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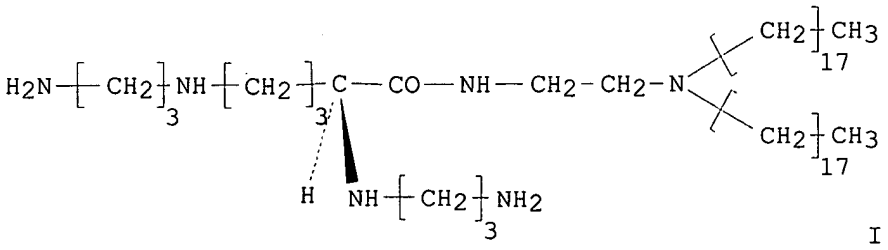


I

AB The invention relates to novel lipopolyamines [H(NH(CH2)a)b]2-nN(H)n(CH2)cX(R)(CH2)dN(H)m[((CH2)eNH)fH]2-m, where R = (CH2)gN(R1)(R2); R1, R2 = independently (un)satd., (un)substituted alkyl; X = N, N(CH2)hC(O)NH, N(CH2)rC(O)O, N(CH2)kNHC(O), N(CH2)kOC(O), CHC(O)NH, CHC(O)O, CHC(O)NH(CH2)lNH, CHCH2NH; [see text for values and combinations of letter subscripts], (including their salts), characterized by a sym., highly flexible lipophilic component with a buffering capacity at physiol. pH, and to their use for funneling biol. active materials such as DNA, RNA, ribozymes, anti-sense DNA, peptides and proteins into eukaryotic cells in vivo or in vitro. Thus, N-BOC-N',N'-dioctadecylethylenediamine was prepd. from N-BOC-ethylenediamine and octadecyl bromide, and reacted with tetra-BOC-carboxyspermine, and the product N-deprotected to give I as its tetra-TFA salt. In in vitro transfection tests of pCVM<Sport>.beta.-Gal with CV-1, Hela S3, and NIH 3T3 cells, liposomes constructed from I and dioleoylphosphatidylethanoamine, dioleoylphosphatidylcholine, cholesterol, or cholesteryl-amine, in

presence or absence of serum, showed relative transfection efficiencies of 66-100%.

ST lipopolyamine prepn octadecylethylenediamine carboxyspermine **transport** liposome transfection

IT Amines, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**polyamines**, nonpolymeric; reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT Transformation, genetic
(prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT Amino acids, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT 107-13-1, 2-Propenenitrile, reactions 112-89-0, Octadecyl bromide 3184-13-2, Ornithine hydrochloride 5003-71-4, 3-Bromopropylamine hydrobromide 57260-73-8 119798-08-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT 83948-53-2P 220170-77-4P 220170-78-5P 220170-79-6P 220170-80-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT 220170-83-2P 220170-84-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT 220170-82-1P 220170-86-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

IT 220170-85-4 **220170-87-6** 220170-88-7
RL: **THU (Therapeutic use); BIOL (Biological study); USES (Uses)**
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

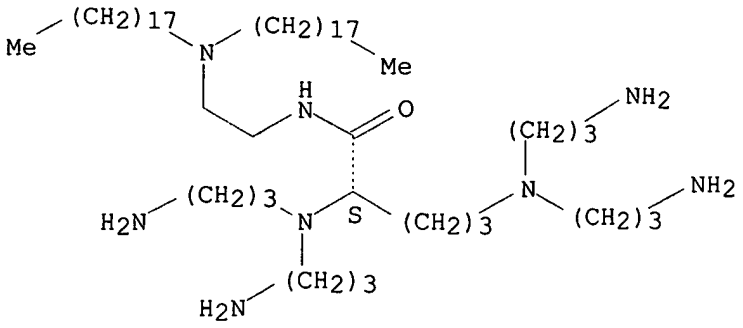
(1) Boehringer Mannheim Gmbh; EP 0544292 A 1993 HCAPLUS
(2) Centre Nat Rech Scient; EP 0394111 A 1990 HCAPLUS
(3) Eltz, H; WO 9700241 A 1997 HCAPLUS
(4) Life Technologies Inc; WO 9405624 A 1994 HCAPLUS
(5) Patrick, D; WO 9703939 A 1997 HCAPLUS
(6) Vical Inc; WO 9116024 A 1991

IT **220170-87-6**
RL: **THU (Therapeutic use); BIOL (Biological study); USES (Uses)**
(reaction of in the prepn. of novel lipopolyamines for use in **transport** liposomes for carrying transfection agents)

RN 220170-87-6 HCAPLUS

CN Pentanamide, 2,5-bis[bis(3-aminopropyl)amino]-N-[2-(dioctadecylamino)ethyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L119 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:414726 HCAPLUS
DN 129:62994
TI Cationic amphiphiles containing amino acid or derivatized amino acid groups for intracellular delivery of therapeutic molecules
IN Harris, David J.; Lee, Edward R.; Siegel, Craig S.; Rowe, Eric A.; Hubbard, Shirley C.
PA Genzyme Corporation, USA
SO U.S., 52 pp., Cont.-in-part of U.S. 5,747,471.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-70
ICS A61K017-28; A61K031-56; A61K048-00; B61F017-28
NCL 514044000
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 14, 32
FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5767099	A	19980616	US 1995-546086	19951020	<--
	US 5650096	A	19970722	US 1994-352479	19941209	<--
	US 5747471	A	19980505	US 1995-540867	19951011	<--
	AU 9732315	A1	19980417	AU 1997-32315	19970610	<--
	AU 736143	B2	20010726			
	EP 1007003	A1	20000614	EP 1997-927989	19970610	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2001500897	T2	20010123	JP 1998-515603	19970610	<--
PRAI	US 1994-352479	A2	19941209	<--		
	US 1995-540867	A2	19951011	<--		
	WO 1997-US9748	W	19970610	<--		

OS MARPAT 129:62994
AB Novel cationic amphiphiles are provided that facilitate **transport** of biol. active (therapeutic) mols. into cells. The amphiphiles contain lipophilic groups derived from steroids and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines, polyalkylamines or amino acids. The products may be used to provide gene therapy and deliver antisense polynucleotides or biol. active polypeptides to cells. For gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation, such as cystic fibrosis. Thus, the carbamate H2N(CH2)3NH(CH2)4N(COCH2NHCO2R)(CH2)3NH2 [R = 3-cholesteryl] was prepd. by treating N-tert-butoxycarbonylglycine N-hydroxysuccinimide ester with N1,N12-di-benzyloxycarbonylspermine, benzyloxycarbonylation at N9, de-tert-butoxycarbonylation, reaction with cholesteryl chloroformate, and

deblocking. The product was effective in enhancing cell transfection efficiency.

ST steroid carbamate **polyamine** amino acid prepn; cell transfection steroid carbamate; gene therapy steroid carbamate

IT Gene therapy
Transformation, genetic
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179074-99-8 179075-00-4 179075-01-5 179075-02-6 179075-05-9
179075-07-1 179075-08-2 179075-10-6 179075-11-7 179075-12-8
179075-13-9 179075-14-0 179075-15-1 179075-16-2 179075-29-7
179075-32-2 179075-33-3 179075-34-4 179075-38-8 179075-39-9
179075-42-4 179075-43-5 179075-50-4 179075-51-5 207386-54-7
209112-46-9 209112-47-0 209112-48-1 **209112-50-5**
RL: BUU (Biological use, unclassified); **BIOL (Biological study)**; **USES (Uses)**
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-25-3P 179075-30-0P 179075-37-7P 179075-40-2P
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-04-8P 179075-31-1P 179075-36-6P 179075-41-3P 179075-44-6P
179075-45-7P 179075-46-8P 179075-47-9P 179075-48-0P 179075-49-1P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 56-18-8, N-(3-Aminopropyl)-1,3-propanediamine 71-44-3, Spermine
80-97-7, Dihydrocholesterol 112-99-2 143-23-7, Bis(6-aminohexyl)amine
628-20-6, 4-Chlorobutyronitrile 910-31-6, Cholesteryl chloride
3392-07-2 4799-67-1, 3-Benzyloxy-1,2-propanediol 7144-08-3,
Cholesteryl chloroformate 14611-34-8 20255-94-1, 1,2-
Dimyristoylglycerol 30189-36-7 51323-71-8, Dodecyl methanesulfonate
89965-56-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 2206-21-5P 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P
103493-12-5P 105793-81-5P 149204-03-5P 179075-52-6P 179075-53-7P
179075-54-8P 179075-55-9P 179075-56-0P 179075-58-2P 179075-59-3P
179075-62-8P 179075-66-2P 179075-67-3P 179075-68-4P 179075-69-5P
179075-70-8P 179075-71-9P 179075-72-0P 179075-73-1P 183249-68-5P
200813-36-1P 202649-06-7P 202649-07-8P 202649-08-9P 209112-59-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amphiphilic steroid carbamates for cell transfection and gene therapy)

IT 179075-63-9P 179075-74-2P 203917-63-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(amphiphilic steroid carbamates for cell transfection and gene therapy)

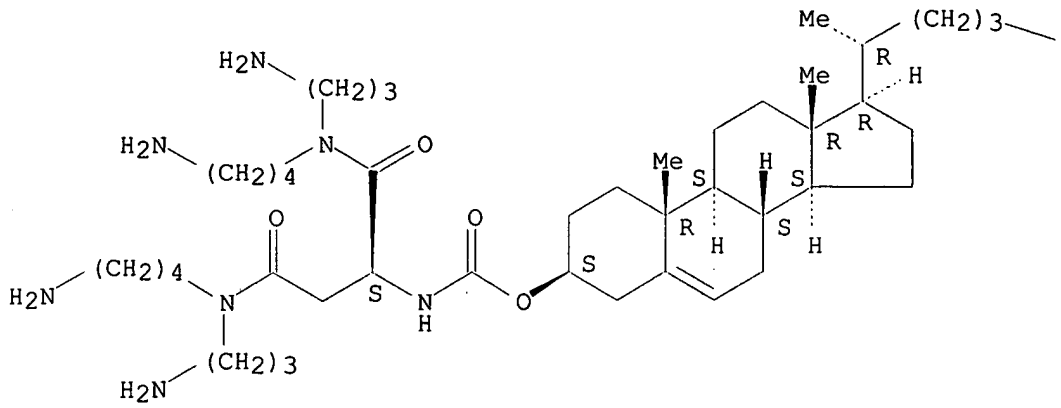
IT **209112-50-5**
RL: BUU (Biological use, unclassified); **BIOL (Biological study)**; **USES (Uses)**
(amphiphilic steroid carbamates for cell transfection and gene therapy)

RN 209112-50-5 HCAPLUS

CN Cholest-5-en-3-ol (3.beta.)-, [(1S)-3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe2

L119 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:282396 HCAPLUS
DN 129:8571
TI Cationic amphiphiles containing steroid lipophilic groups for intracellular delivery of therapeutic molecules
IN Siegel, Craig S.; Harris, David J.; Lee, Edward R.; Hubbard, Shirley C.; Cheng, Seng H.; Eastman, Simon J.; Marshall, John; Scheule, Ronald K.; Lane, Mathieu B.; Rowe, Eric A.
PA Genzyme Corp., USA
SO U.S., 53 pp., Cont.-in-part of U.S. Ser. No. 352,479.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K048-00
ICS A61K031-56; A61K031-70; B01F017-28
NCL 514044000
CC **63-5** (Pharmaceuticals)
Section cross-reference(s): 32
FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5747471	A	19980505	US 1995-540867	19951011	<--
	US 5650096	A	19970722	US 1994-352479	19941209	<--
	US 6071890	A	20000606	US 1995-545473	19951019	<--
	US 5719131	A	19980217	US 1995-546110	19951020	<--
	US 5767099	A	19980616	US 1995-546086	19951020	<--
	US 5840710	A	19981124	US 1995-546087	19951020	<--
	US 5910487	A	19990608	US 1995-546205	19951020	<--
	CA 2205968	AA	19960620	CA 1995-2205968	19951208	<--
	WO 9618372	A2	19960620	WO 1995-US16174	19951208	<--

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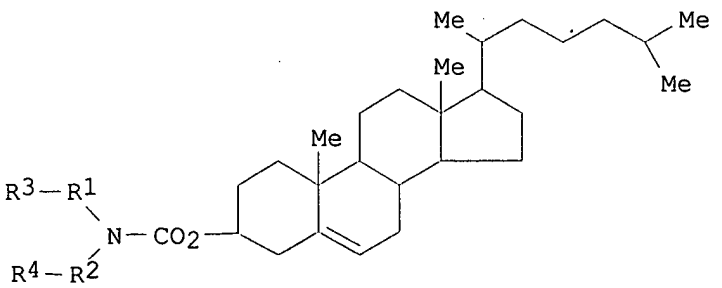
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR,

NE, SN, TD, TG

AU 9645161	A1	19960703	AU 1996-45161	19951208	<--
AU 716706	B2	20000302			
EP 799059	A1	19971008	EP 1995-943769	19951208	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
JP 10510813	T2	19981020	JP 1995-519236	19951208	<--
US 5783565	A	19980721	US 1996-595375	19960201	<--
US 5948767	A	19990907	US 1996-679514	19960712	<--
US 5939401	A	19990817	US 1996-680354	19960715	<--
US 6331524	B1	20011218	US 1997-835213	19970407	<--
WO 9813026	A1	19980402	WO 1997-US9748	19970610	<--
W: AU, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
AU 9732315	A1	19980417	AU 1997-32315	19970610	<--
AU 736143	B2	20010726			
EP 1007003	A1	20000614	EP 1997-927989	19970610	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001500897	T2	20010123	JP 1998-515603	19970610	<--
US 6383814	B1	20020507	US 1999-228232	19990111	<--
AU 734980	B2	20010628	AU 1999-57180	19991101	<--
AU 9957180	A1	20000106			
PRAI US 1994-352479	A2	19941209	<--		
US 1995-4344P	P	19950926	<--		
US 1995-4399P	P	19950927	<--		
US 1995-540867	A2	19951011	<--		
US 1995-545473	A	19951019	<--		
US 1995-546087	A1	19951020	<--		
US 1995-546110	A2	19951020	<--		
US 1995-564087	A1	19951020	<--		
WO 1995-US16174	W	19951208	<--		
US 1996-661279	A2	19960610	<--		
US 1996-667122	B2	19960620	<--		
US 1996-668676	B1	19960625	<--		
WO 1997-US9748	W	19970610	<--		

OS MARPAT 129:8571

GI



I

AB Novel cationic amphiphiles I (R1, R2 = alkylamine, polyalkylamine; R3, R4 = H satd. or unsatd. aliph. group; R1 and R2 may be the same or different) are provided that facilitate **transport** of biol. active (therapeutic) mols. into cells. Thus, N1,N8-dicarbobenzoxyspermidine was treated with cholesteryl chloroformate followed by hydrogenolysis to give N4-spermidine cholesteryl carbamate. The amphiphiles contain lipophilic groups derived from steroids, from mono or dialkylamines, or from ether or ester-linked alkyl groups, and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines or polyalkylamines. There are provided also therapeutic compns. prepd. typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols.

Therapeutic mols. that can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic compns. of the invention include providing gene therapy, and delivery of antisense polynucleotides or biol. active polypeptides to cells. With respect to therapeutic compns. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation.

ST cationic amphiphile steroid lipophilic group; drug delivery therapeutic cationic amphiphile steroid

IT Drug delivery systems
Gene therapy
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT Steroids, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT **Biological transport**
(drug; cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 179075-25-3P 179075-30-0P 179075-31-1P 179075-32-2P 179075-35-5P
179075-36-6P 179075-37-7P 179075-40-2P 203917-63-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 179075-00-4 179075-01-5 179075-02-6 179075-04-8 179075-05-9
179075-07-1 179075-08-2 **179075-09-3** 179075-10-6
179075-11-7 179075-12-8 179075-13-9 179075-14-0 179075-15-1
179075-29-7 179075-33-3 179075-34-4 179075-38-8 179075-39-9
179075-41-3 179075-42-4 179075-43-5 179075-44-6 179075-45-7
179075-46-8 179075-47-9 179075-48-0 179075-49-1 179075-50-4
207386-54-7 207386-55-8
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 71-44-3, Spermine 85-41-6, Phthalimide 107-13-1, Acrylonitrile, reactions 112-99-2 910-31-6, Cholesteryl chloride 4799-67-1
7144-08-3, Cholesteryl chloroformate 14611-34-8 89965-56-0
179075-73-1 202649-07-8 207386-52-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

IT 80-97-7P, Dihydrocholesterol 628-20-6P, 4-Chlorobutyronitrile
2206-21-5P 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P
103493-12-5P 105793-81-5P 179075-53-7P 179075-62-8P 179075-66-2P
179075-67-3P 179075-68-4P 179075-69-5P 179075-70-8P 179075-71-9P
179075-72-0P 183249-68-5P 200813-36-1P 202649-06-7P 207386-53-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cationic amphiphiles contg. steroid lipophilic groups for

intracellular delivery of therapeutic mols.)

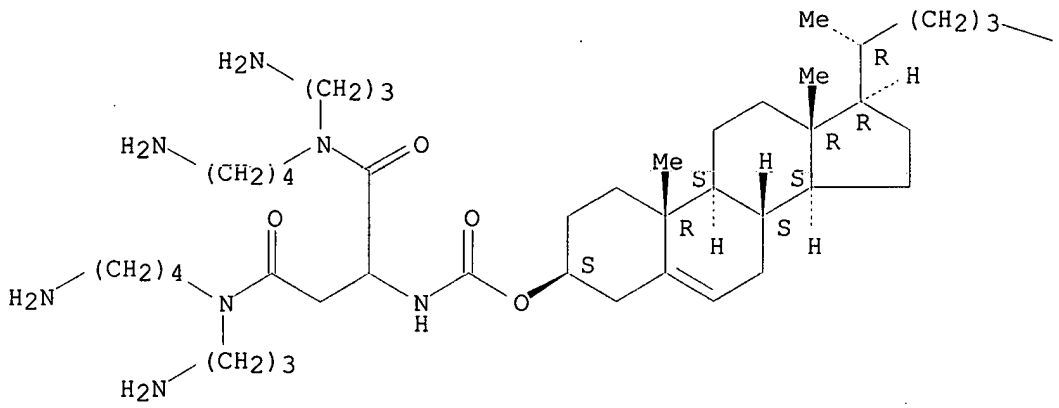
IT **179075-09-3**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; **BIOL (Biological study)**; **USES (Uses)**
(cationic amphiphiles contg. steroid lipophilic groups for intracellular delivery of therapeutic mols.)

RN 179075-09-3 HCAPLUS

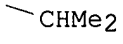
CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L119 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:268467 HCAPLUS

DN 128:321804

TI Preparation of spermine analogs for use as **polyamine transport inhibitors**

IN **Poulin, Richard; Audette, Marie; Charest-Gaudrealt, Rene**

PA Universite Laval, Can.; Poulin, Richard; Audette, Marie; Charest-Gaudrealt, Rene

SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C211-13

CC 31-6 (Alkaloids)
Section cross-reference(s): 1, 34, **63**

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9817623	A2	19980430	WO 1997-IB1651	19971022 <--
WO 9817623	A3	19980903		

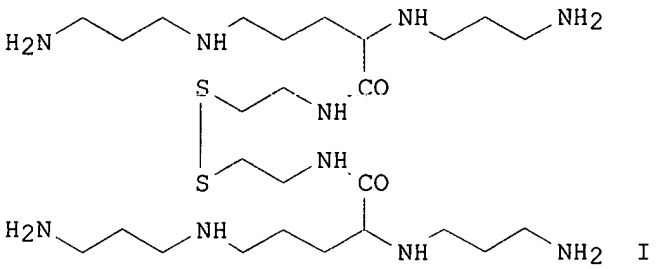
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,

LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG,
KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

US 6083496	A	20000704	US 1996-735130	19961022	<--
CA 2241339	AA	19980430	CA 1997-2241339	19971022	<--
AU 9857752	A1	19980515	AU 1998-57752	19971022	<--
EP 876327	A2	19981111	EP 1997-953991	19971022	<--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRAI US 1996-735130 A 19961022 <--
WO 1997-IB1651 W 19971022 <--
OS MARPAT 128:321804
GI



AB Spermine analogs, such as R1NHCR2R3(CH2)wNH(CH2)xCH(CONHR)(CH2)yNH(CH2)zCR 2R3NHR1 [R = H, moiety which cannot be captured by **polyamine transporter**; R1 = R2 = R3 = H, alkyl; w = 2, 3; z = 2, 3; x = integer from 1 to n; n = integer from 3 to 6; yr = n minus x], were prepd. for therapeutic use as novel **inhibitors** of **polyamine transport**. The main feature of this class of **transport inhibitors** is to incorporate a linker or side chain that prevents the uptake of **polyamines** and helps to conjugate **polyamine** analogs to form dimers with high **inhibitory** potency against **polyamine** uptake. These new compds. incorporate features that were designed to maximize their chem. and metabolic stability and their ability to bind to the **polyamine transporter**, and to minimize their toxicity by preventing their absorption by the cells. The purpose of such **inhibitors** is to prevent the uptake or salvaging of circulating **polyamines** by rapidly proliferating cells such as tumor cells, in order to potentiate the effect of therapeutic **inhibitors** of **polyamine** biosynthesis such as Eflornithine. Thus, spermine analog I was prepd. starting from ornithine hydrochloride and cystamine dihydrochloride. Prepd. compds. underwent pharmacol. testing as well as testing to detn. **inhibition** of cell proliferation of tumor cell lines such as ZR-75-1 human breast cancer cells and CHO-K1 Chinese hamster ovary cells.

ST spermine analog prepn **polyamine transport inhibitor**; anticancer agent spermine analog prepn

IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamines**, nonpolymeric; prepn. of spermine analogs for use as **polyamine transport inhibitors**)

IT Antitumor agents
Biological transport
(prepn. of spermine analogs for use as **polyamine**

transport inhibitors)

IT **206760-63-6P** 206760-65-8P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

IT 71-44-3DP, Spermine, analogs 206760-64-7P 206760-66-9P **206760-67-0P 206760-68-1P 206760-69-2P 206760-70-5P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**
(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

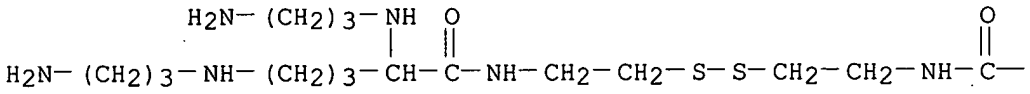
IT 56-17-7, Cystamine dihydrochloride 144-48-9, Iodoacetamide 3483-12-3, Dithiothreitol 6211-16-1, Ornithine dihydrochloride 24424-99-5, Di-tert-butyl dicarbonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

IT 119798-07-1P 186002-24-4P 206760-71-6P 206760-72-7P 206760-73-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

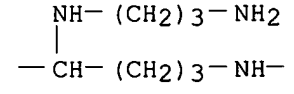
IT **206760-63-6P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); RACT (Reactant or reagent); **USES (Uses)**
(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

RN 206760-63-6 HCAPLUS
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



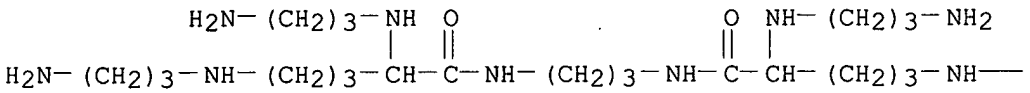
IT **206760-67-0P 206760-68-1P 206760-69-2P 206760-70-5P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; **BIOL (Biological study)**; PREP (Preparation); **USES (Uses)**

(prepn. of spermine analogs for use as **polyamine transport inhibitors**)

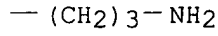
RN 206760-67-0 HCAPLUS

CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



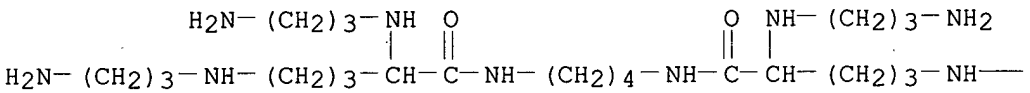
PAGE 1-B



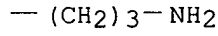
RN 206760-68-1 HCAPLUS

CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



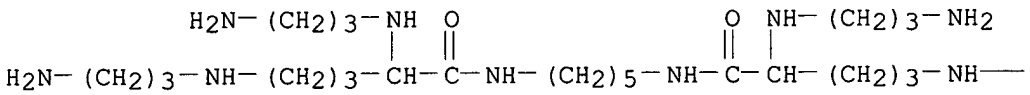
PAGE 1-B



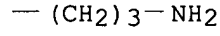
RN 206760-69-2 HCAPLUS

CN Pentanamide, N,N'-1,5-pentanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



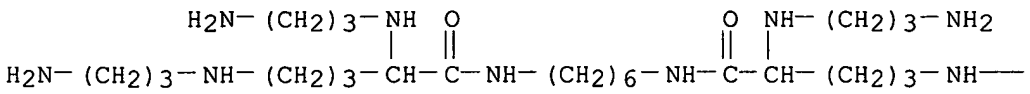
PAGE 1-B



RN 206760-70-5 HCAPLUS

CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

L119 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:269701 HCAPLUS
DN 126:340122
TI Transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers
AU Sakai, Naomi; Matile, Stefan
CS Department of Chemistry, Georgetown University, Washington, DC, 20057-1227, USA
SO Tetrahedron Letters (**1997**), 38(15), 2613-2616
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
CC 6-1 (General Biochemistry)
OS CASREACT 126:340122
AB A series of amphiphilic **polyamine** dendrimers was efficiently prepd. from cholestamine to probe the hypothesis that an increasing no. of ammonium cations attached to a hydrophobic anchoring group should increasingly facilitate transmembrane ion **transport**. Results from **transport** expts. using large unilamellar vesicles are consistent with this new concept.
ST **transport** membrane bilayer **polyamine** amphiphilic
IT Membrane, biological
(bilayer; transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)
IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(**polyamines**, nonpolymeric; transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)
IT **Biological transport**
(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)
IT 189879-66-1 189879-67-2 189879-68-3
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)
IT 2206-20-4P 189879-70-7P 189879-73-0P 189879-79-6P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or

reagent)
(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT **189879-77-4P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation); PROC (Process)
(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

IT **189879-77-4P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation); PROC (Process)
(transmembrane ion **transport** mediated by amphiphilic **polyamine** dendrimers)

RN 189879-77-4 HCAPLUS

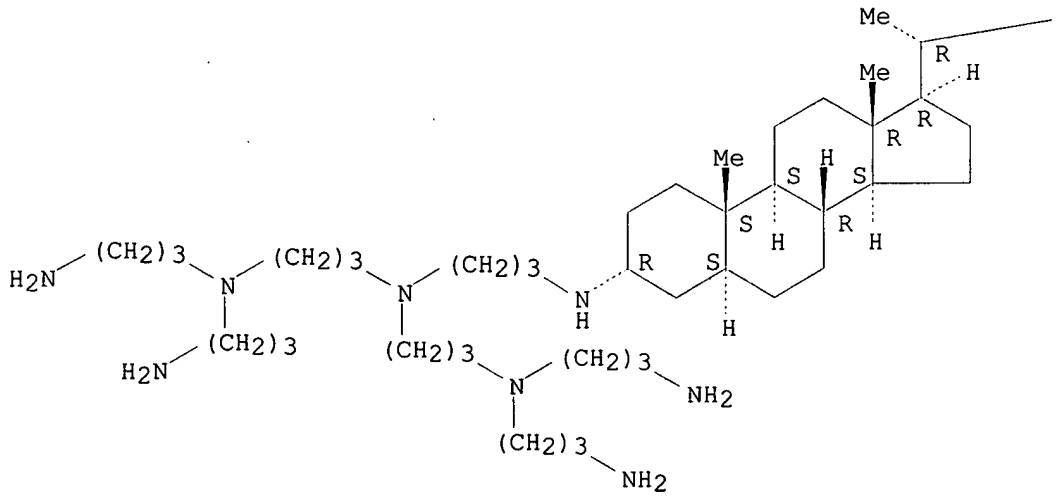
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-[[(3.alpha.,5.alpha.)-cholestan-3-yl]amino]propyl]-, octakis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

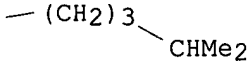
CRN 189879-76-3
CMF C48 H98 N8

Absolute stereochemistry.

PAGE 1-A

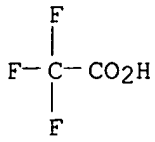


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L119 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:681591 HCAPLUS
DN 126:42328
TI 2,2'-Dithiobis(N-ethyl-spermine-5-carboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system
AU Huber, Maria; Pelletier, Joele G.; Torossian, Krikor; Dionne, Patricia; Gamache, Isabelle; **Charest-Gaudreault, Rene; Audette, Marie; Poulin, Richard**
CS Laboratory Molecular Endocrinology, Laval University Medical Research Center, Ste. Foy, QC, G1V 4G2, Can.
SO Journal of Biological Chemistry (**1996**), 271(44), 27556-27563
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
CC 1-6 (Pharmacology)
AB We have synthesized 2,2'-dithiobis(N-ethyl-spermine-5-carboxamide) (DESC), its thiol monomer (MESC), and the mixed MESC-cysteamine disulfide (DEASC) as potential **inhibitors** of **polyamine transport** in mammalian cells. DESC was the most potent antagonist of spermine **transport** in ZR-75-1 human breast cancer cells, with Ki values of 5.0.+-.0.7, 80.+-.31, and 16.+-.3 .mu.M for DESC, MESC, and DEASC, resp. DESC also strongly blocked putrescine and spermidine uptake in ZR-75-1 cells (Ki = 1.6.+-.0.5 and 2.7.+-.1.1 .mu.M, resp.). While DESC and MESC were purely competitive **inhibitors** of putrescine **transport**, DEASC was a mixed competitive/noncompetitive antagonist. Remarkably, DESC was virtually impermeant in ZR-75-1 cells despite its low Ki toward **polyamine transport**. The marked difference in affinity between DESC and MESC was essentially due to the tail-to-tail juxtaposition of two spermine-like structures, suggesting that dimeric ligands of the **polyamine transporter** might simultaneously interact with more than one binding site. While DESC strongly decreased the initial rate of [3H]spermidine **transport**, even a 40-fold molar excess of antagonist could not completely abolish intracellular spermidine accumulation. Moreover, as little as 0.3 .mu.M spermidine fully restored growth in ZR-75-1 cells treated with an **inhibitor** of **polyamine** biosynthesis in the presence of 50 .mu.M DESC, thus emphasizing the importance of uptake of trace amts. of exogenous **polyamines**. Thus, reducing the exogenous supply of **polyamines** with a potent competitive **inhibitor** may be kinetically inadequate to block replenishment of the **polyamine** pool in **polyamine**-depleted tumor cells that display high **transport** capacity. These results demonstrate that **polyamine** analogs cross-linked into a dimeric structure such as DESC interact with high affinity with the mammalian **polyamine** carrier without being used as substrates. These novel properties provide a framework for the design of specific irreversible **inhibitors** of the **polyamine transporter**, which should present advantages over competitive antagonists for an efficient blockade of **polyamine transport** in tumor cells.
ST antitumor dithiobisethylsperminecarboxamide deriv membrane **polyamine transport**
IT Antitumor agents.

Biological transport
Cell membrane
Neoplasm
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT Antitumor agents
(mammary gland; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT Mammary gland
(neoplasm, **inhibitors**; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT Amines, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**polyamines**, nonpolymeric; dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT **184895-97-4P** 184895-98-5P 184895-99-6P 184896-00-2P 184896-01-3P 184896-02-4P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT 71-44-3, Spermine 110-60-1, Putrescine 124-20-9, Spermidine
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT 51-85-4, Cystamine 56-17-7, Cystamine dihydrochloride 6211-16-1, Ornithine dihydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT 124076-28-4P 184896-03-5P 184896-04-6P 184896-05-7P 184896-06-8P 184896-07-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

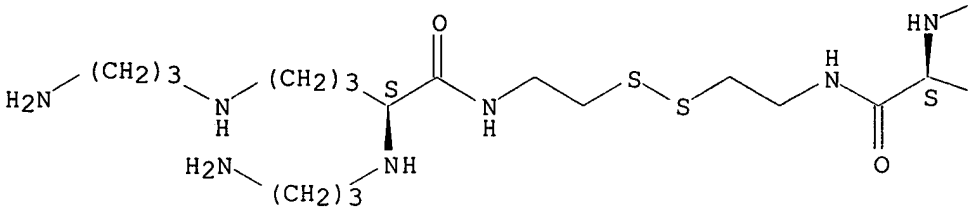
IT 184896-08-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

IT **184895-97-4P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **BIOL (Biological study)**; PREP (Preparation)
(dithiobis(ethylsperminecarboxamide) is a high affinity, membrane-impermeant antagonist of the mammalian **polyamine transport** system)

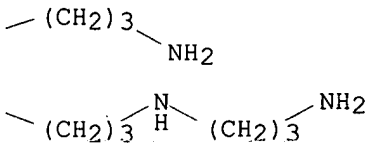
RN 184895-97-4 HCAPLUS
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L119 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:456098 HCAPLUS
DN 125:107063
TI Cationic amphiphiles and plasmids for intracellular delivery of therapeutic molecules
IN Siegel, Craig S.; Harris, David J.; Lee, Edward R.; Hubbard, Shirley C.; Cheng, Seng H.; Eastman, Simon J.; Marshall, John; Scheule, Ronald K.; Yew, Nelson S.; et al.
PA Genzyme Corporation, USA
SO PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 63
FAN.CNT 11

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9618372	A2	19960620	WO 1995-US16174	19951208 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5650096	A	19970722	US 1994-352479	19941209 <--
US 5747471	A	19980505	US 1995-540867	19951011 <--
US 6071890	A	20000606	US 1995-545473	19951019 <--
AU 9645161	A1	19960703	AU 1996-45161	19951208 <--
AU 716706	B2	20000302		
EP 799059	A1	19971008	EP 1995-943769	19951208 <--
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JP 10510813	T2	19981020	JP 1995-519236	19951208 <--
AU 9732315	A1	19980417	AU 1997-32315	19970610 <--
AU 736143	B2	20010726		
EP 1007003	A1	20000614	EP 1997-927989	19970610 <--

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	US 2002013282	A1	20020131		US 1998-166074	19981005 <--
PRAI	US 1994-352479	A	19941209	<--		
	US 1995-4344P	P	19950926	<--		
	US 1995-4399P	P	19950927	<--		
	US 1995-540867	A	19951011	<--		
	US 1995-545473	A	19951019	<--		
	WO 1995-US16174	W	19951208	<--		
	WO 1997-US9748	W	19970610	<--		

OS MARPAT 125:107063

AB Novel cationic amphiphiles are provided that facilitate **transport** of biol. active (therapeutic) mols. into cells. The amphiphiles contain lipophilic groups derived from steroids, from mono or dialkylamines, or from alkyl or acyl groups; and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines or polyalkylamines. Thus, N4-spermidine cholesteryl carbamate provided an .apprx.20-fold enhancement of the transfection ability of plasmid pCMVHI-CAT (chloramphenicol acetyltransferase-encoding) in mice. There are provided also therapeutic compns. prepd. typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols. Therapeutic mols. that can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic compns. of the invention include providing gene therapy, and delivery of antisense polynucleotides of biol. active polypeptides to cells. With respect to therapeutic compns. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation. Several vectors were constructed for improved delivery of the gene the cystic fibrosis transmembrane conductance regulator (CFTR) under control of the human cytomegalovirus promoter/enhancer during cationic amphiphile-mediated gene transfer. Addnl., targeting of organs for gene therapy by i.v. administration of therapeutic compns. is described. Syntheses are described for N4-spermine cholesteryl carbamate, N4-(N'-cholesteryl carbamate glycineamide)-spermine, N4-spermidine-2,3-dilauryloxypropylamine, and N4-spermine-2,3-dilauryloxypropylamine.

ST cationic amphiphile transfection plasmid gene therapy; inflammation cytokine gene therapy plasmid transfection; cystic fibrosis CFTR gene therapy plasmid

IT Cystic fibrosis
Inflammation
Inflammation inhibitors
Pharmaceuticals
Transformation, genetic
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Lymphokines and Cytokines
Ribozymes
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Gene
Ribonucleic acids, messenger
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(encoding therapeutic protein; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Plasmid and Episome
(pCF1; cationic amphiphiles and plasmids for intracellular delivery of

therapeutic mols.)
IT Plasmid and Episome
(pCMV-CFTR; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Plasmid and Episome
(pMyc4-CFTR; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Glycophosphoproteins
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(CFTR (cystic fibrosis transmembrane conductance regulator), cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Gene, animal
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DHFR, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Ribonucleic acids
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antisense, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Gene, animal
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(c-myc, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Amphiphiles
(cationic, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Deoxyribonucleic acids
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(complementary, encoding therapeutic protein; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Deoxyribonucleic acids
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(complementary, antisense, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancer element, from human cytomegalovirus, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Therapeutics
(geno-, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interleukin 1, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interleukin 1 receptor antagonist, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)
IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(interleukin 11, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interleukin 2, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interleukin 6, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interleukin 8, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Lymphokines and Cytokines
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(monocyte chemoattractant protein 1, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ori, from human .beta.-globin gene, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Plasmid and Episome
(pCF2, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyadenylation signal, from bovine growth hormone, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(promoter, from human cytomegalovirus, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Genetic element
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transposon Tn903, plasmids constructed with; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT Phosphoproteins
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(tumor suppressor, p53, cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 9041-92-3, .alpha.1-Antitrypsin 83869-56-1, Granulocyte-macrophage colony-stimulating factor 123626-67-5, Endothelin-1 124861-55-8, Proteinase inhibitor, TIMP-2 140208-24-8, Proteinase inhibitor, TIMP-1
RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-63-9P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 80-97-7, Dihydrocholesterol 85-41-6, Phthalimide 100-46-9, Benzylamine, reactions 107-13-1, 2-Propenenitrile, reactions 112-99-2 628-20-6, 4-Chlorobutyronitrile 910-31-6, Cholesteryl chloride 4799-67-1, 3-Benzyloxy-1,2-propanediol 14611-34-8 30189-36-7 51323-71-8, Dodecylmethanesulfonate 179075-72-0
RL: RCT (Reactant)
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 17677-18-8P 32450-33-2P 78217-67-1P 92312-22-6P 179075-61-7P 179075-62-8P 179075-64-0P 179075-65-1P 179075-66-2P 179075-67-3P 179075-68-4P 179075-69-5P 179075-70-8P 179075-71-9P 179075-73-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 2462-63-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-lipid for transfection; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 57-50-1, biological studies 59-23-4, Galactose, biological studies 63-42-3 69-65-8, Mannitol 69-79-4 99-20-7, Trehalose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(excipient; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 3392-07-2
RL: RCT (Reactant)
(synthesis of (cholesteryl carbamate glycineamide)spermine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-54-8P 179075-55-9P 179075-56-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of (cholesteryl carbamate glycineamide)spermine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 20255-94-1 89965-56-0 179075-58-2
RL: RCT (Reactant)
(synthesis of spermidine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-57-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of spermidine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 71-44-3, Spermine 7144-08-3, Cholesteryl chloroformate
RL: RCT (Reactant)
(synthesis of spermine cholesteryl carbamate; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-52-6P 179075-53-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of spermine cholesteryl carbamate; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-59-3
RL: RCT (Reactant)
(synthesis of spermine dilauryloxypropylamine; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179075-60-6
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transfection-enhancing agent; anionic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT 179074-99-8 179075-00-4 179075-01-5 179075-02-6 179075-03-7 179075-04-8 179075-05-9 179075-06-0 179075-07-1 179075-08-2 **179075-09-3** 179075-10-6 179075-11-7 179075-12-8

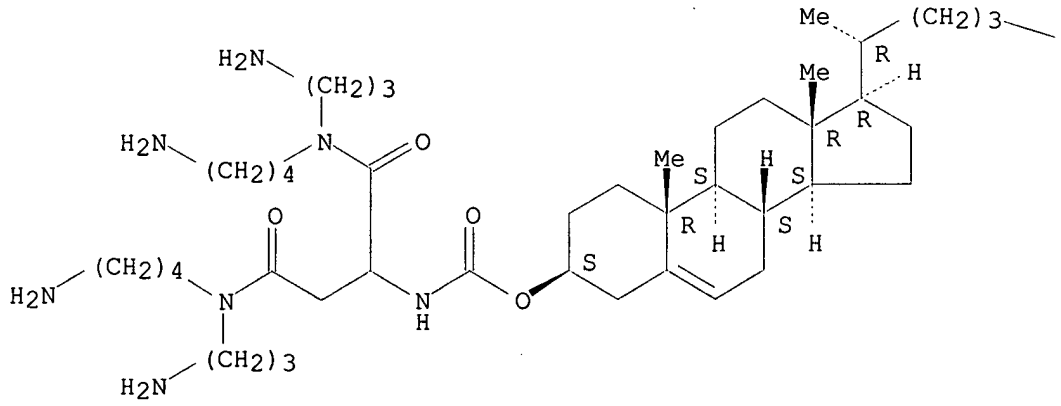
179075-13-9 179075-14-0 179075-15-1 179075-16-2 179075-17-3
179075-18-4 179075-19-5 179075-20-8 179075-21-9 179075-22-0
179075-23-1 179075-24-2 179075-25-3 179075-26-4 179075-27-5
179075-28-6 179075-29-7 179075-30-0 179075-31-1 179075-32-2
179075-33-3 179075-34-4 179075-35-5 179075-36-6 179075-37-7
179075-38-8 179075-39-9 179075-40-2 179075-41-3 179075-42-4
179075-43-5 179075-44-6 179075-45-7 179075-46-8 179075-47-9
179075-48-0 179075-49-1 179075-50-4 179075-51-5 179075-74-2
RL: **BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)**
(transfection-enhancing agent; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

IT **179075-09-3**
RL: **BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)**
(transfection-enhancing agent; cationic amphiphiles and plasmids for intracellular delivery of therapeutic mols.)

RN 179075-09-3 HCAPLUS
CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe2

L119 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:463054 HCAPLUS
DN 119:63054
TI Calcium receptor-active molecules
IN Nemeth, Edward F.; Van Wagenen, Bradford C.; Balandrin, Manuel F.
PA NPS Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-566

ICS G01N033-567; C07C211-02; C07C211-16; C07C211-27; C07H021-00; C07K005-00; C07K007-00; C12N015-12; A61K037-02

CC 1-10 (Pharmacology)
Section cross-reference(s): 9, **63**

FAN.CNT 9

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9304373	A1	19930304		WO 1992-US7175	19920821	<--
	W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US						
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG						
	AU 9225889	A1	19930316		AU 1992-25889	19920821	<--
	AU 673500	B2	19961114				
	JP 06510531	T2	19941124		JP 1992-504650	19920821	<--
	JP 2728564	B2	19980318				
	EP 657029	A1	19950614		EP 1992-919933	19920821	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE						
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	JP 09328420	A2	19971222		JP 1996-232130	19920821	<--
	JP 11221095	A2	19990817		JP 1998-313631	19920821	<--
	JP 3256502	B2	20020212				
	RU 2147574	C1	20000420		RU 1994-20394	19920821	<--
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	CN 1067550	B	20010627				
	IL 102917	A1	20001206		IL 1992-102917	19920823	<--
	ZA 9206360	A	19930330		ZA 1992-6360	19920824	<--
	NO 9400581	A	19940425		NO 1994-581	19940221	<--
	AU 9671977	A1	19970220		AU 1996-71977	19961125	<--
	AU 711247	B2	19991007				
	AU 9931226	A1	19990722		AU 1999-31226	19990524	<--
PRAI	US 1991-749451	A2	19910823	<--			
	US 1992-834044	A2	19920211	<--			
	US 1992-934161	A2	19920821	<--			
	JP 1992-504650	A3	19920821	<--			
	JP 1996-232165	A3	19920821	<--			
	JP 1998-313631	A3	19920821	<--			
	WO 1992-US7175	A	19920821	<--			
	US 1993-141248	A	19931022	<--			
	US 1994-292827	A	19940819	<--			
	AU 1994-80872	A3	19941021	<--			

OS MARPAT 119:63054

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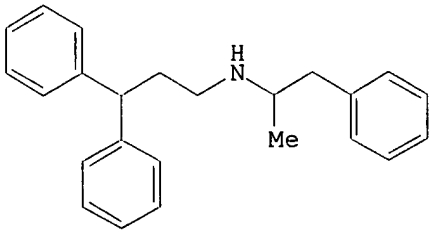


I

AB Methods, compns., and compds. are disclosed for treating a patient having a disease characterized by an abnormal level of component(s), the activity of which is regulated or affected by the activity of .gtoreq.1 Ca2+ receptors. The compds. act as agonists or antagonists of the Ca2+

receptors, preferably selective to receptors on parathyroid cells, bone osteoclasts, juxtaglomerular kidney cells, proximal tubule kidney cells, keratinocytes, parafollicular thyroid cells, and placental trophoblasts. A method for diagnosis of a disease comprises identifying the no. and/or location of Ca2+ receptors and making a comparison to that of normal subjects. Methods for identifying useful therapeutic mols. are also disclosed. Structure-function (intracellular Ca2+-mobilizing) studies were done on aminoglycosides and other compds. on various cells. Recombinant Ca2+ receptor protein mRNAs were expressed in Xenopus oocytes. Compd. NPS 449 (I) caused a concn.-dependent inhibition of bone resorption with an IC50 of 10 .mu.M.

ST calcium receptor agonist antagonist

IT Blood
Blood serum
(calcium of, redn. of, by calcium receptor-active NPS 467)

IT Osteoclast
(calcium receptor on)

IT Trophoblast
(calcium receptor on, of placenta)

IT Antihypertensives
(calcium receptor-active mols.)

IT Pharmaceutical analysis
(calcium receptor-active mols. identification in, screening method for)

IT Immunoassay
(calcium receptors detn. by, for disease diagnosis)

IT Neoplasm
(diagnosis of, calcium receptors detn. in)

IT Gene, animal
RL: BIOL (Biological study)
(for calcium receptor)

IT Ribonucleic acids, messenger
RL: BIOL (Biological study)
(for exogenous calcium receptor, chloride ion conductance increase in Xenopus oocyte elicitation by)

IT Neoplasm inhibitors
(for hypercalcemia-causing tumors, calcium receptor-active mols.)

IT Protamines
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(intracellular calcium-mobilizing activity of)

IT Diagnosis
(of calcium-related diseases or conditions, calcium receptors detn. in)

IT Xenopus
Xenopus laevis
(oocytes of, chloride ion conductance increase in, exogenous calcium receptor mRNA elicitation of)

IT Parathyroid gland
(parathyroid hormone secretion by cells of, intracellular calcium levels-affecting substance inhibition of)

IT Peptides, biological studies
RL: BIOL (Biological study)
(pos.-charged, calcium receptor-active mols.)

IT Bone, metabolism
(resorption of, intracellular calcium levels-affecting substance inhibition of)

IT Antibodies
RL: BIOL (Biological study)
(to calcium receptors, for immunoassay for disease diagnosis)

IT Osteoporosis
(treatment of, with calcium receptor-active mols.)

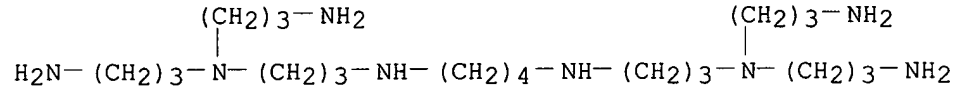
IT Placenta
(trophoblasts of, calcium receptor on)

IT Thyroid gland, composition

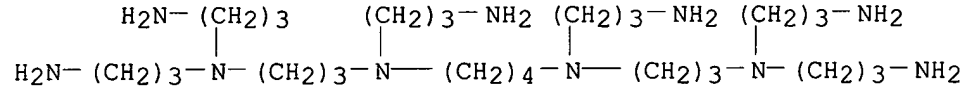
(C cell, calcium receptor on)
IT Bone, disease
(Paget's, treatment of, with calcium receptor-active mols.)
IT Amines, biological studies
RL: BIOL (Biological study)
(alkaryl, calcium receptor-active mols.)
IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(amino, intracellular calcium-mobilizing activity of)
IT **Polyamines**
RL: BIOL (Biological study)
(branched, calcium receptor-active mols.)
IT Ion channel blockers
Ion channel openers
(calcium, pharmaceuticals)
IT Receptors
RL: BIOL (Biological study)
(calcium, substances binding and active with, of osteoclasts and other cells)
IT Molecular structure-biological activity relationship
(calcium-mobilizing, intracellular, of aminoglycosides and other **polyamines**)
IT Glycerides, biological studies
RL: BIOL (Biological study)
(di-, intracellular calcium levels-affecting substance causing increase in)
IT Kidney, composition
(juxtaglomerular cell, calcium receptor on)
IT Skin, composition
(keratinocyte, calcium receptor on)
IT Parathyroid gland
(neoplasm, diagnosis of, calcium receptors detn. in)
IT Egg
(oocyte, chloride ion conductance increase in, of Xenopus, exogenous calcium receptor mRNA elicitation of)
IT Pharmaceutical dosage forms
(oral, of calcium receptor-active NPS 467 isomer, blood serum calcium lowering with)
IT **Amines**, biological studies
RL: BIOL (Biological study)
(**poly**-, cyclic, calcium receptor-active mols.)
IT Hyperparathyroidism
(primary, treatment of, with calcium receptor-active mols.)
IT Kidney, composition
(proximal tubule, calcium receptor on cell of)
IT Hyperparathyroidism
(secondary, treatment of, with calcium receptor-active mols.)
IT **Biological transport**
(**translocation**, of intracellular calcium, calcium receptor-active substances effect on)
IT 51-61-6, Dopamine, biological studies 7683-59-2, Isoproterenol
RL: BIOL (Biological study)
(cAMP formation stimulated by, intracellular calcium levels-affecting substance inhibition of)
IT 148740-51-6
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(calcilytic activity of, on parathyroid cells)
IT 390-64-7 13042-18-7 108448-58-4 114753-78-5 133805-32-0 148717-48-0 148717-50-4
RL: BIOL (Biological study)
(calcium receptor-active mol.)

IT 108393-62-0D, derivs.
RL: BIOL (Biological study)
(calcium receptor-active mols.)
IT 16887-00-6, Chloride ion, biological studies
RL: PRP (Properties)
(conductance of, increase in, in Xenopus oocytes injected with mRNA for calcium receptor)
IT 60-92-4, CAMP
RL: FORM (Formation, nonpreparative)
(formation of, dopamine- or isoproterenol-stimulated, intracellular calcium levels-affecting substance inhibition of)
IT 16561-29-8, Phorbol myristate acetate 34807-41-5, Mezerein 90365-57-4, (-)-Indolactam V
RL: BIOL (Biological study)
(intracellular calcium levels-affecting substance activity inhibition by)
IT 141436-78-4, Protein kinase C
RL: BIOL (Biological study)
(intracellular calcium levels-affecting substance activity inhibition by activator of)
IT 88269-39-0, Inositol-1,4,5-triphosphate
RL: BIOL (Biological study)
(intracellular calcium levels-affecting substance causing increase in)
IT 7681-49-4, Sodium fluoride, biological studies
RL: BIOL (Biological study)
(intracellular calcium levels-affecting substance inhibition by)
IT 7439-96-5, Manganese, biological studies
RL: BIOL (Biological study)
(intracellular calcium-mobilizing activity of)
IT 52-53-9 57-92-1, Streptomycin, biological studies 71-44-3, Spermine 112-24-3, Triethylenetetramine 112-57-2, Tetraethylenepentamine 119-04-0, Neomycin B 124-20-9, Spermidine 154-21-2, Lincomycin 296-35-5, Hexacyclen 1403-66-3, Gentamicin 2783-17-7, 1,12-Diaminododecane 4067-16-7, Pentaethylenehexamine 4696-76-8, Bekanamycin 8063-07-8, Kanamycin 16662-47-8 24937-47-1 25104-18-1 25212-18-4 38000-06-5 42399-41-7, Diltiazem 57818-92-5, TMB-8 87955-89-3 105029-41-2, Argiotoxin 636 111944-83-3, Argiotoxin 659 115976-91-5, Philanthotoxin 433 128549-96-2, Agatoxin 489 128549-97-3 139750-76-8, Budmunchiamine A **148717-51-5** 148717-52-6 148717-53-7 **148740-50-5**
RL: **BAC (Biological activity or effector, except adverse)**; **BIOL (Biological study)**
(intracellular calcium-mobilizing activity of)
IT 159149-75-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of and bovine parathyroid cell calcium receptor activation by)
IT 148717-54-8P 148717-55-9P 148717-56-0P 148740-52-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and bovine parathyroid cell calcium receptor activation by)
IT 148717-47-9P 148717-49-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and calcium receptor activity of)
IT 13042-18-7DP, Fendiline, analogs 13042-18-7P, Fendiline
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, calcium receptor-active substances in relation to)
IT 5586-73-2
RL: RCT (Reactant)
(reaction of, with acetophenone, in prepn. of calcium receptor-active substance)
IT 98-86-2, Acetophenone, reactions
RL: RCT (Reactant)
(reaction of, with bisphenylpropylamine, in prepn. of calcium

receptor-active substance)
IT 2038-57-5, 3-Phenylpropylamine 18655-48-6
RL: RCT (Reactant)
(reaction of, with methoxyacetophenone)
IT 586-37-8, 3'-Methoxyacetophenone
RL: RCT (Reactant)
(reaction of, with phenylpropylamine)
IT 9002-64-6, Parathyroid hormone
RL: BIOL (Biological study)
(secretion of, by parathyroid cell, intracellular calcium levels-affecting substance inhibition of)
IT 9007-12-9, Calcitonin
RL: BIOL (Biological study)
(secretion of, stimulation of, with calcium receptor-binding substance)
IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(substances increasing or blocking intracellular)
IT **148717-51-5 148740-50-5**
RL: **BAC (Biological activity or effector, except adverse); BIOL (Biological study)**
(intracellular calcium-mobilizing activity of)
RN 148717-51-5 HCAPLUS
CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,17-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)



RN 148740-50-5 HCAPLUS
CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,8,13,17-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)



L119 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS
AN 1992:105949 HCAPLUS
DN 116:105949
TI .alpha.-Methyl **polyamines**: metabolically stable spermidine and spermine mimics capable of supporting growth in cells depleted of **polyamines**
AU Lakanen, John R.; Coward, James K.; Pegg, Anthony E.
CS Dep. Chem., Univ. Michigan, Ann Arbor, MI, 48109-1055, USA
SO J. Med. Chem. (**1992**), 35(4), 724-34
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
CC 26-9 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 6
AB In order to assess the tolerance of the target enzyme spermine synthase for .alpha.-substituents on the aminopropyl moiety of the substrate spermidine, 1-methylspermidine (I) was synthesized. I is a poor substrate for spermine synthase and is not a substrate for spermidine N1-acetyltransferase, suggesting that .alpha.-methylated **polyamines** might be metabolically stable and therefore useful tools for studying **polyamine** effects in intact cells. On the

basis of initial cellular results with I, 1-methylspermine (II) and 1,12-dimethylspermine (III) were also synthesized. When added to cells (L1210, SV-3T3, or HT29) depleted of both putrescine and spermidine by prior treatment with .alpha.-(difluoromethyl)ornithine (IV), these .alpha.-methylated **polyamines** were able to restore cell growth to that obsd. in the absence of IV. In accord with the enzyme data noted above, metabolic studies indicated a slow conversion of I to II, but no metab. of III in these cells. It was concluded from these results that the .alpha.-methylated **polyamines** are able to substitute for the natural **polyamines**, spermidine and spermine in crit. biochem. processes which involve **polyamines** for continued cell growth. In accord with the hypothesis, preliminary data indicate that I and III are as effective as spermidine and spermine, resp., in promoting the conversion of B-DNA to Z-DNA.

ST methylspermidine prepn enzyme substrate; methylspermine prepn enzyme substrate; spermine synthase substrate methylspermidine; spermidine acetyltransferase substrate methylspermidine; **polyamine** transport system methylspermidine

IT **Biological transport**
(of **polyamines**, methylspermines and methylspermidines in study of)

IT 64885-84-3, Spermidine-N1-acetyltransferase
RL: RCT (Reactant)
(methylspermidines and methylspermines as substrates for)

IT 137945-95-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deblocking of)

IT 66917-07-5P 137945-96-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrazinolysis of)

IT 66917-06-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation of)

IT 138051-81-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with aminobutylphthalimide)

IT 62146-62-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with aminobutyric acid)

IT 5394-18-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with azide)

IT 35517-18-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with azidobutyrate)

IT 18523-47-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with azidobutyrylbutanediamine)

IT 137964-65-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with azidopropionate)

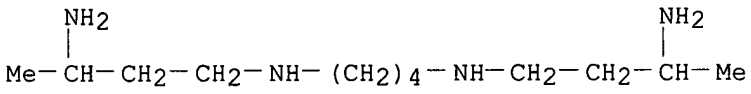
IT 137945-97-2P 137945-98-3P 137945-99-4P 137946-00-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)

IT 137945-92-7P 137945-93-8P **137945-94-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 137946-01-1P 137946-02-2P **137946-03-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as spermidine acetyltransferase substrate)

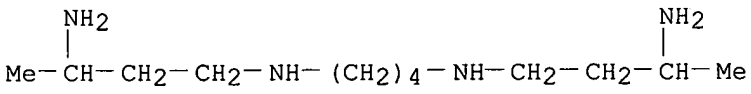
IT 71-44-3DP, Spermine, Me derivs. 124-20-9DP, Spermidine, Me derivs.
RL: PREP (Preparation)
(prepn. of, as spermidine acetyltransferase substrates)

IT 110-60-1, Putrescine
RL: RCT (Reactant)
(reaction of, with aminobutyric acid)
IT 79-10-7, Acrylic acid, reactions 3724-65-0, Crotonic acid
RL: RCT (Reactant)
(reaction of, with azide)
IT 2835-82-7
RL: RCT (Reactant)
(reaction of, with butanediamine deriv.)
IT **137945-94-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 137945-94-9 HCAPLUS
CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis-, tetrahydrochloride (9CI)
(CA INDEX NAME)



● 4 HCl

IT **137946-03-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as spermidine acetyltransferase substrate)
RN 137946-03-3 HCAPLUS
CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis- (9CI) (CA INDEX NAME)



=> fil reg
FILE 'REGISTRY' ENTERED AT 11:32:35 ON 01 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 28 JUN 2002 HIGHEST RN 435268-39-6
DICTIONARY FILE UPDATES: 28 JUN 2002 HIGHEST RN 435268-39-6

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

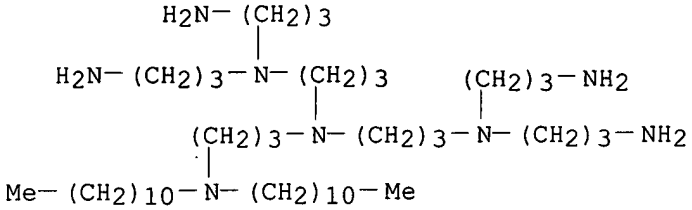
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot l120

L120 ANSWER 1 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **272463-38-4** REGISTRY
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(diundecylamino)propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C43 H96 N8
SR CA
LC STN Files: CA, CAPLUS

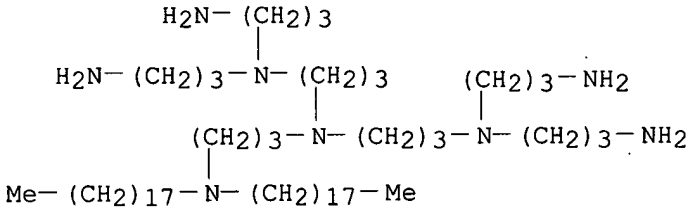


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:22412

L120 ANSWER 2 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **272462-73-4** REGISTRY
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-(dioctadecylamino)propyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C57 H124 N8
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

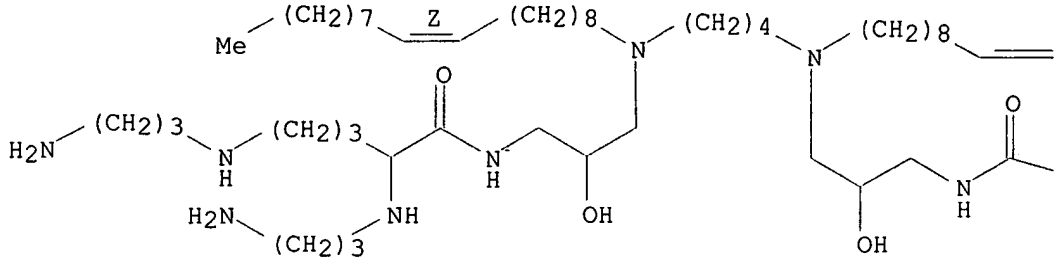
REFERENCE 1: 133:22412

L120 ANSWER 3 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **268554-12-7** REGISTRY
CN Pentanamide, N,N'-[1,4-butanediylbis[[(9Z)-9-octadecenylimino](2-hydroxy-3,1-propanediyl)]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)

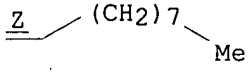
FS STEREOSEARCH
MF C68 H142 N12 O4
SR CA
LC STN Files: CA, CAPLUS

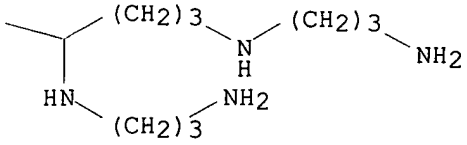
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B





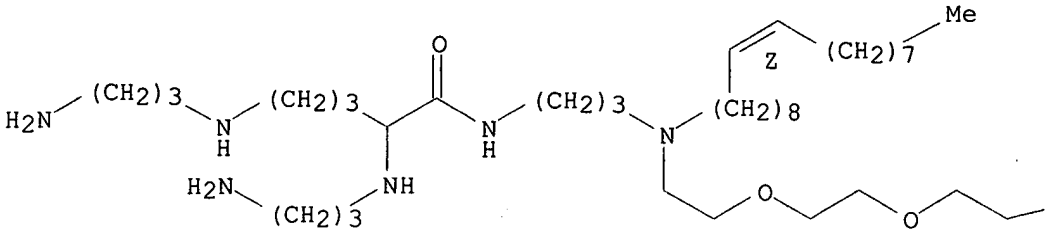
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 4 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **268539-58-8** REGISTRY
CN Pentanamide, N,N'-[4,13-di-(9Z)-9-octadecenyl-7,10-dioxa-4,13-diazahexadecane-1,16-diyl]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C70 H146 N12 O4
SR CA
LC STN Files: CA, CAPLUS

Double bond geometry as shown.

PAGE 1-A



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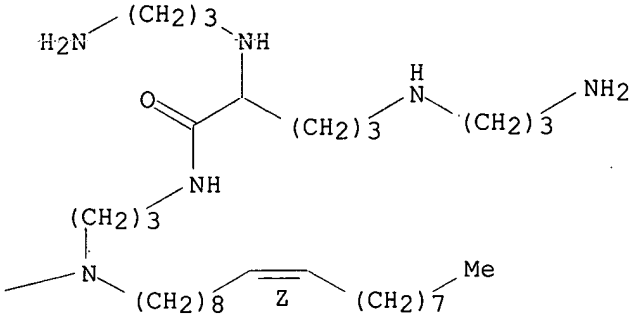


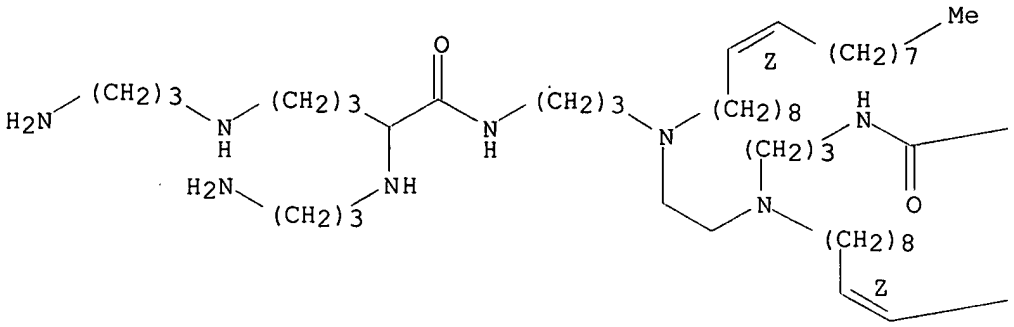
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

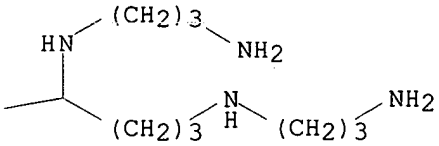
L120 ANSWER 5 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **268539-54-4** REGISTRY
CN Pentanamide, N,N'-[1,2-ethanediylbis[[(9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C66 H138 N12 O2
SR CA
LC STN Files: CA, CAPLUS

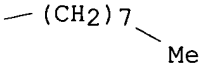
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B





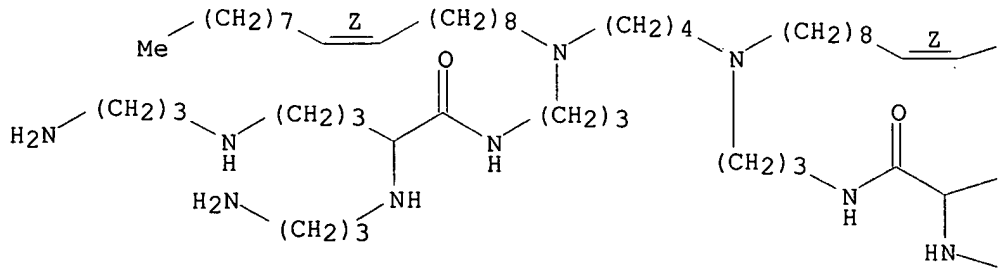
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 6 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **268539-53-3** REGISTRY
CN Pentanamide, N,N'-[1,4-butanediylbis[[(9Z)-9-octadecenylimino]-3,1-propanediyl]]bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C68 H142 N12 O2
SR CA
LC STN Files: CA, CAPLUS

Double bond geometry as shown.

PAGE 1-A



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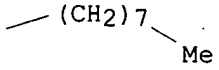
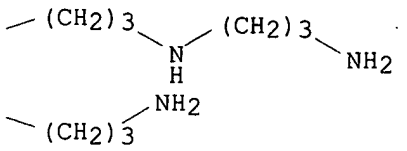
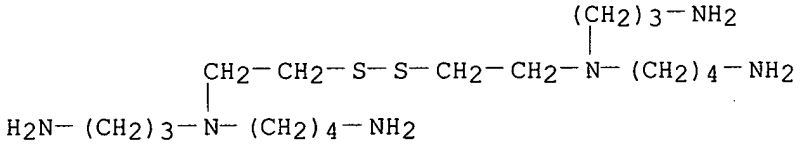




1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:334312

L120 ANSWER 7 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **247187-67-3** REGISTRY
CN 1,4-Butanediamine, N,N''-(dithiodi-2,1-ethanediyl)bis[N-(3-aminopropyl)-(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H44 N6 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

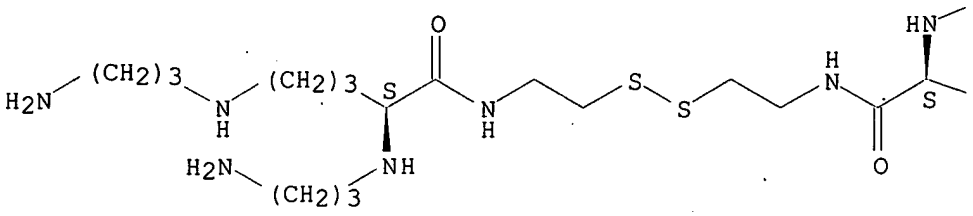
REFERENCE 1: 133:38223

REFERENCE 2: 131:307091

L120 ANSWER 8 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **247187-66-2** REGISTRY
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, octahydrochloride, (2S,2'S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H60 N10 O2 S2 . 8 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (184895-97-4)

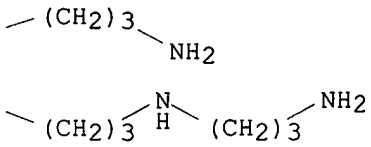
Absolute stereochemistry.

PAGE 1-A



●8 HCl

PAGE 1-B



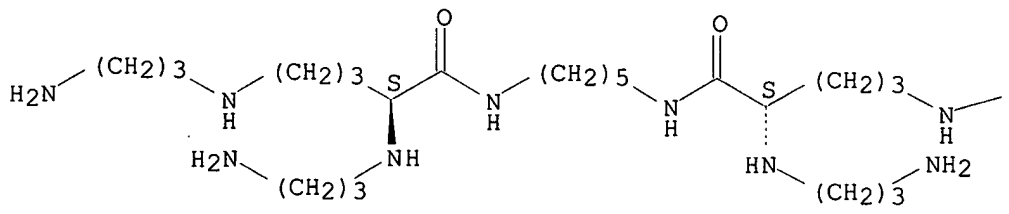
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

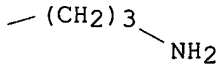
L120 ANSWER 9 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **247187-65-1** REGISTRY
CN Pentanamide, N,N'-1,5-pentanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H62 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

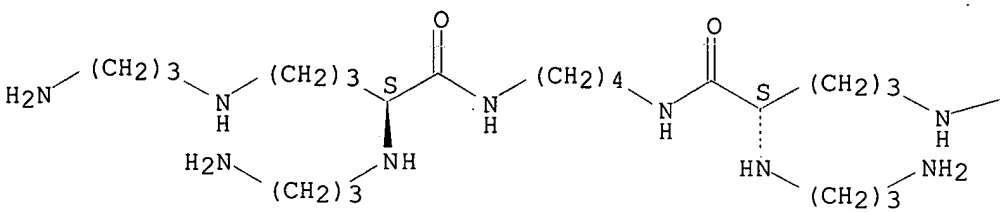
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

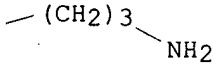
L120 ANSWER 10 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **247187-64-0** REGISTRY
CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H60 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

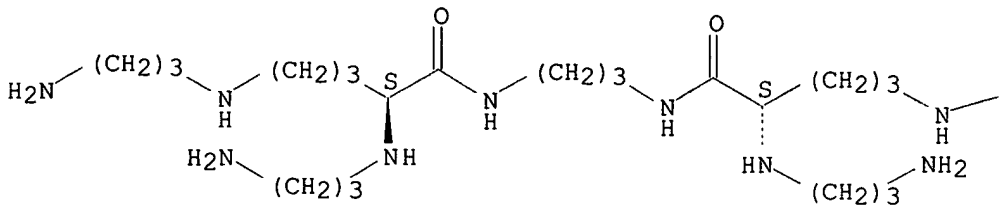
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

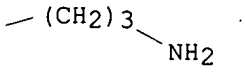
L120 ANSWER 11 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **247187-63-9** REGISTRY
CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H58 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

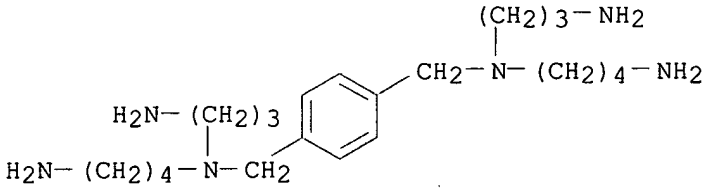


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:307091

L120 ANSWER 12 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-25-8** REGISTRY
CN 1,4-Benzenedimethanamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)
MF C22 H44 N6 . 6 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



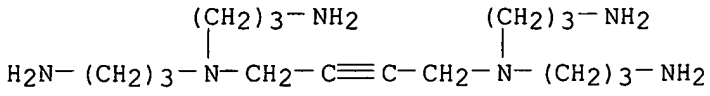
●6 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 13 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-24-7** REGISTRY
CN 2-Butyne-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C16 H36 N6
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

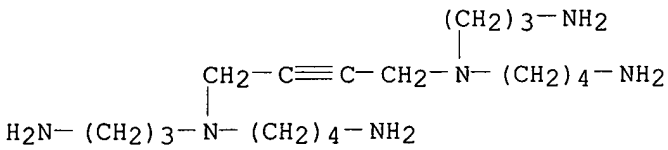


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 14 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-23-6** REGISTRY
CN 2-Butyne-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H40 N6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



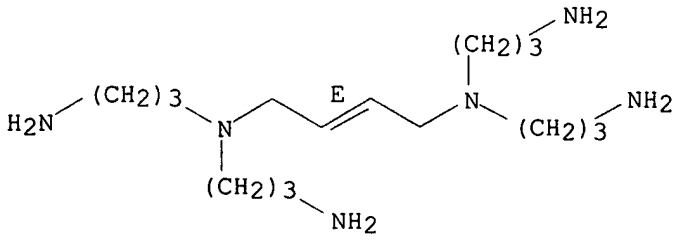
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 15 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-22-5** REGISTRY
CN 2-Butene-1,4-diamine, N,N,N',N'-tetrakis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H38 N6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Double bond geometry as shown.



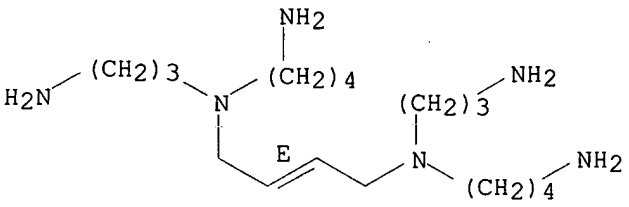
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 16 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-21-4** REGISTRY
CN 2-Butene-1,4-diamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, (2E)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C18 H42 N6
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Double bond geometry as shown.

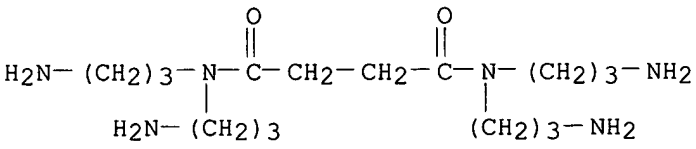


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 17 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-20-3** REGISTRY
CN Butanediamide, N,N,N',N'-tetrakis(3-aminopropyl)-, tetrahydrochloride (9CI) (CA INDEX NAME)
MF C16 H36 N6 O2 . 4 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



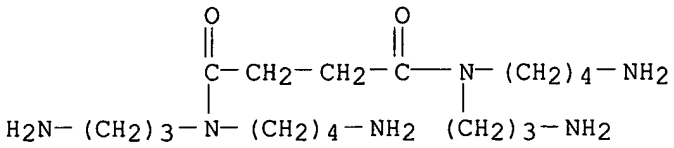
●4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 18 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-19-0** REGISTRY
CN Butanediamide, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-,

tetrahydrochloride (9CI) (CA INDEX NAME)
MF C18 H40 N6 O2 . 4 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

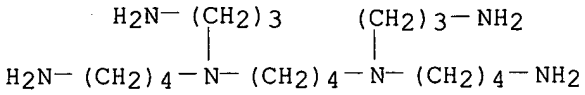


●4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 19 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **244033-18-9** REGISTRY
CN 1,4-Butanediamine, N,N'-bis(4-aminobutyl)-N,N'-bis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)
MF C18 H44 N6 . 6 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



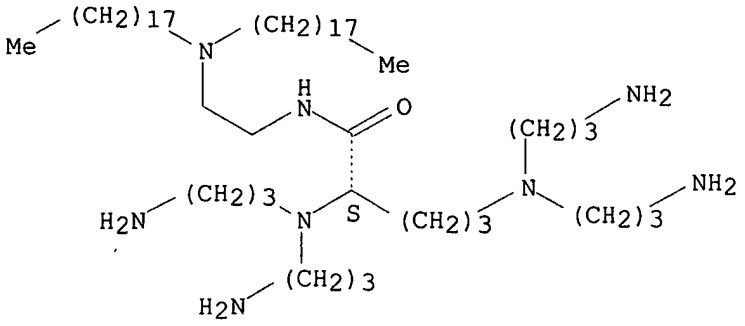
●6 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

L120 ANSWER 20 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **220170-87-6** REGISTRY
CN Pentanamide, 2,5-bis[bis(3-aminopropyl)amino]-N-[2-(dioctadecylamino)ethyl]-, (2S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C55 H118 N8 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



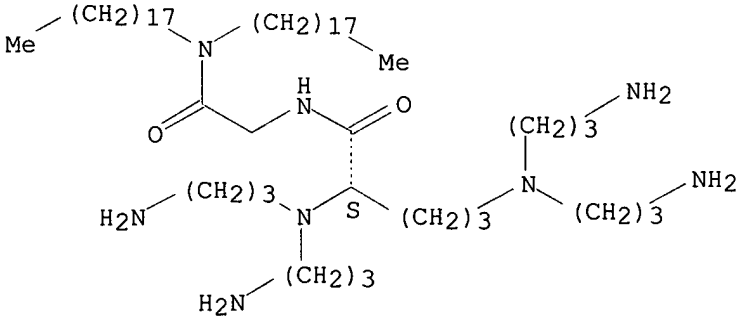
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:153974

L120 ANSWER 21 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **219304-01-5** REGISTRY
CN Glycinamide, N2,N2,N5,N5-tetrakis(3-aminopropyl)-L-ornithyl-N,N-dioctadecyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C55 H116 N8 O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

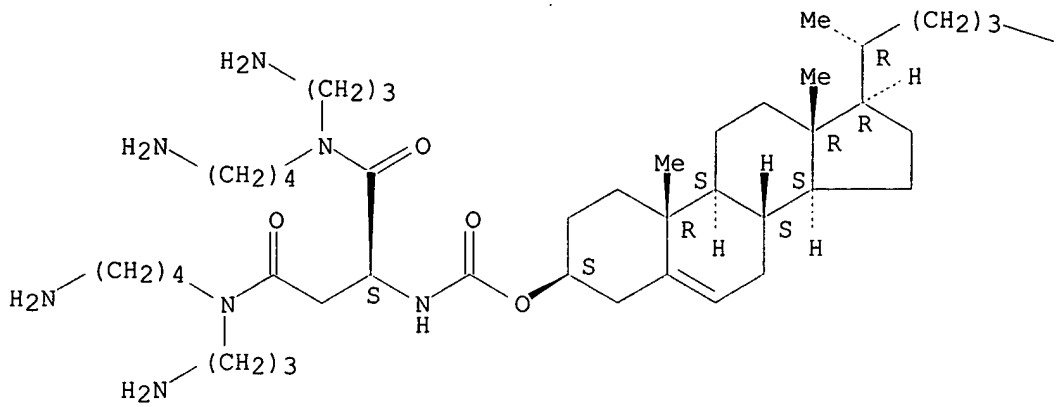
REFERENCE 1: 132:122935

L120 ANSWER 22 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **209112-50-5** REGISTRY
CN Cholest-5-en-3-ol (3.beta.)-, [(1S)-3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C46 H85 N7 O4
SR CA

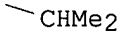
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

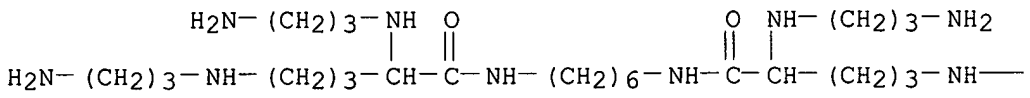


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

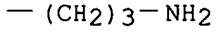
REFERENCE 1: 129:62994

L120 ANSWER 23 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **206760-70-5** REGISTRY
CN Pentanamide, N,N'-1,6-hexanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C28 H64 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

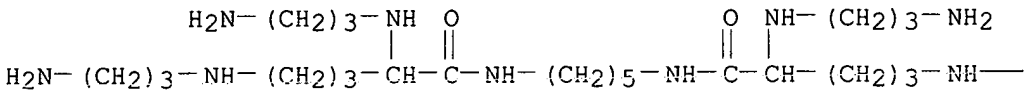
REFERENCE 1: 133:38223

REFERENCE 2: 131:307091

REFERENCE 3: 128:321804

L120 ANSWER 24 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **206760-69-2** REGISTRY
CN Pentanamide, N,N'-1,5-pentanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H62 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

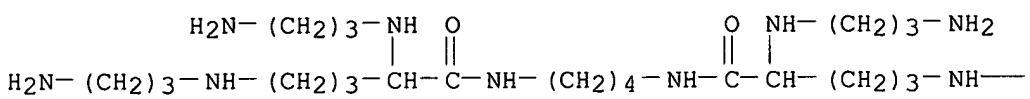
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 25 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **206760-68-1** REGISTRY
CN Pentanamide, N,N'-1,4-butanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H60 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

— $(CH_2)_3-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

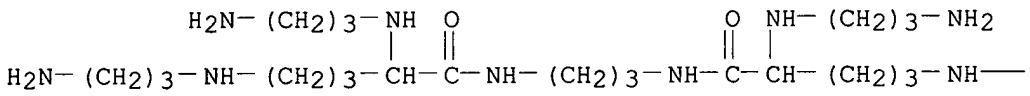
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 26 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **206760-67-0** REGISTRY
CN Pentanamide, N,N'-1,3-propanediylbis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C25 H58 N10 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B

— $(CH_2)_3-NH_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

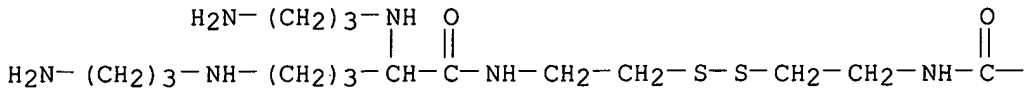
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

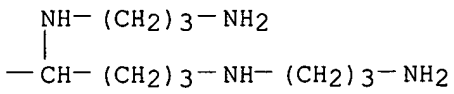
REFERENCE 2: 128:321804

L120 ANSWER 27 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **206760-63-6** REGISTRY
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C26 H60 N10 O2 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B



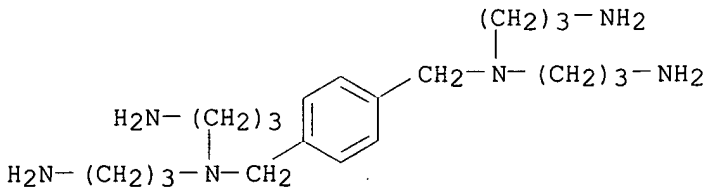
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

REFERENCE 2: 128:321804

L120 ANSWER 28 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **201859-92-9** REGISTRY
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)
MF C20 H40 N6 . 6 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (189076-31-1)



● 6 HCl

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:160331

REFERENCE 2: 131:228866

REFERENCE 3: 128:135724

L120 ANSWER 29 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **189879-77-4** REGISTRY
CN 1,3-Propanediamine, N,N-bis(3-aminopropyl)-N'-[3-[bis(3-aminopropyl)amino]propyl]-N'-[3-[[(3.alpha.,5.alpha.)-cholestan-3-yl]amino]propyl]-, octakis(trifluoroacetate) (9CI) (CA INDEX NAME)
FS STEREOSEARCH

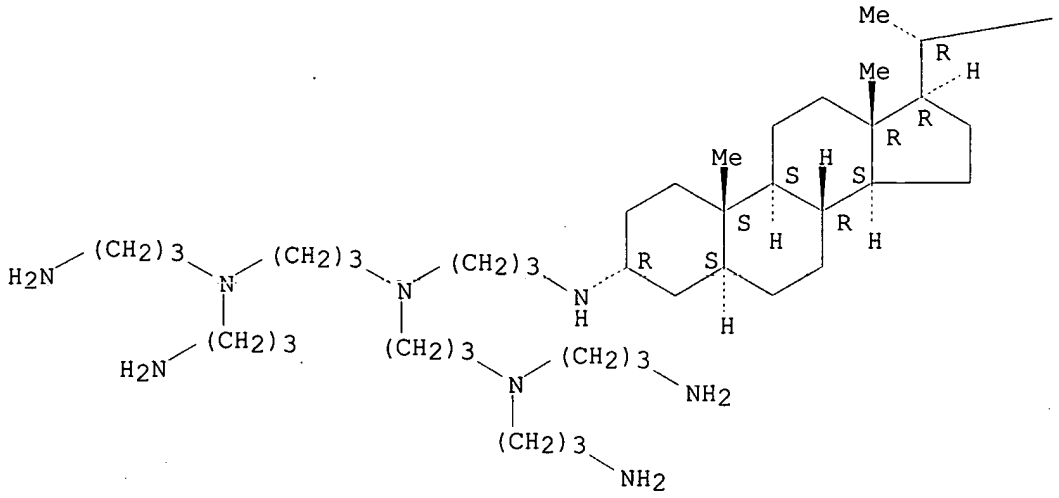
MF C48 H98 N8 . 8 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, CASREACT

CM 1

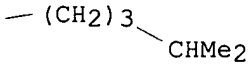
CRN 189879-76-3
CMF C48 H98 N8

Absolute stereochemistry.

PAGE 1-A

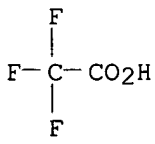


PAGE 1-B



CM 2

CRN 76-05-1
CMF C2 H F3 O2

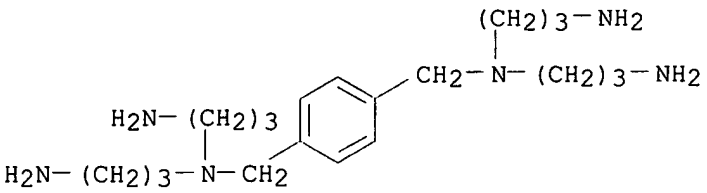


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:340122

L120 ANSWER 30 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **189076-31-1** REGISTRY
CN 1,4-Benzenedimethanamine, N,N,N',N'-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD

MF C20 H40 N6
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:38223

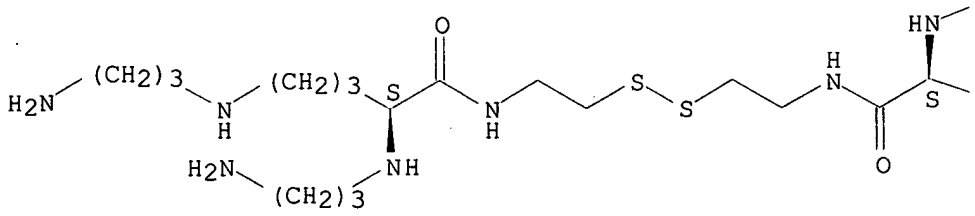
REFERENCE 2: 131:307091

REFERENCE 3: 126:293343

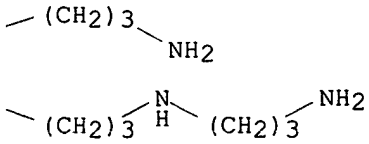
L120 ANSWER 31 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **184895-97-4** REGISTRY
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, (2S,2'S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pentanamide, N,N'-(dithiodi-2,1-ethanediyl)bis[2,5-bis[(3-aminopropyl)amino]-, [S-(R*,R*)]-
FS STEREOSEARCH
MF C26 H60 N10 O2 S2
CI COM
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

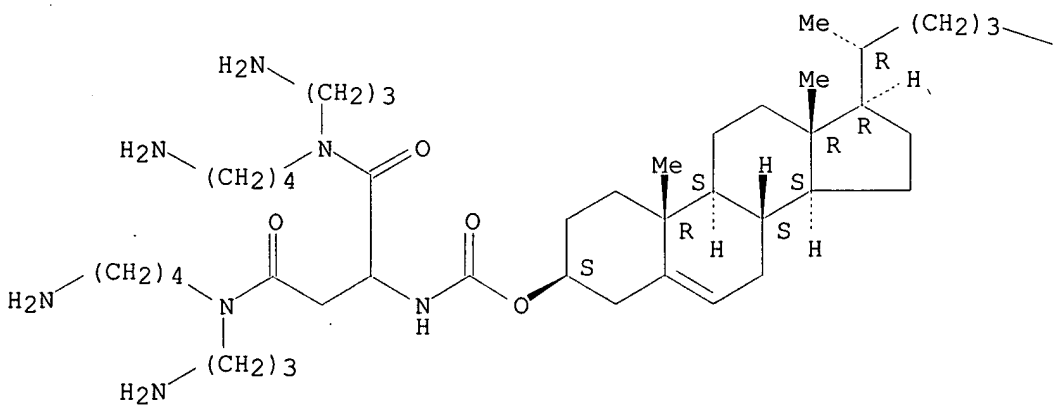
REFERENCE 1: 131:307091

REFERENCE 2: 126:42328

L120 ANSWER 32 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **179075-09-3** REGISTRY
CN Cholest-5-en-3-ol (3.beta.)-, [3-[(4-aminobutyl)(3-aminopropyl)amino]-1-[[(4-aminobutyl)(3-aminopropyl)amino]carbonyl]-3-oxopropyl]carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C46 H85 N7 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CHMe2

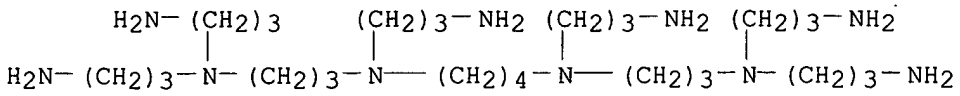
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:8571

REFERENCE 2: 125:107063

L120 ANSWER 33 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **148740-50-5** REGISTRY
CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,8,13,17-tetrakis(3-aminopropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NPS 381
FS 3D CONCORD
MF C28 H68 N10

SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:45937

REFERENCE 2: 132:203164

REFERENCE 3: 132:88193

REFERENCE 4: 130:119576

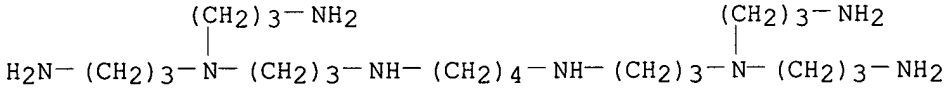
REFERENCE 5: 129:49631

REFERENCE 6: 128:30379

REFERENCE 7: 122:1057

REFERENCE 8: 119:63054

L120 ANSWER 34 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **148717-51-5** REGISTRY
CN 4,8,13,17-Tetraazaeicosane-1,20-diamine, 4,17-bis(3-aminopropyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN NPS 382
FS 3D CONCORD
MF C22 H54 N8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:203164

REFERENCE 2: 132:88193

REFERENCE 3: 130:119576

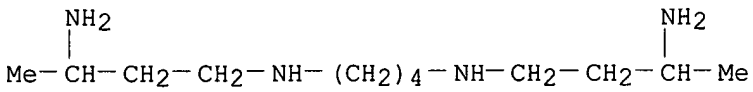
REFERENCE 4: 129:49631

REFERENCE 5: 128:30379

REFERENCE 6: 122:1057

REFERENCE 7: 119:63054

L120 ANSWER 35 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **137946-03-3** REGISTRY
CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C12 H30 N4
CI COM
SR CA
LC STN Files: BEILSTEIN*, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:73053

REFERENCE 2: 134:237682

REFERENCE 3: 133:164201

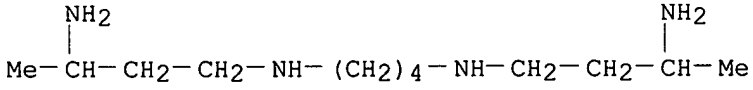
REFERENCE 4: 130:153469

REFERENCE 5: 123:252414

REFERENCE 6: 121:227393

REFERENCE 7: 116:105949

L120 ANSWER 36 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **137945-94-9** REGISTRY
CN 1,3-Butanediamine, N1,N1'-1,4-butanediylbis-, tetrahydrochloride (9CI) (CA INDEX NAME)
MF C12 H30 N4 . 4 Cl H
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)
CRN (137946-03-3)



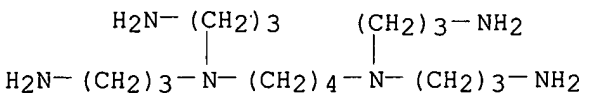
4 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:105949

L120 ANSWER 37 OF 37 REGISTRY COPYRIGHT 2002 ACS
RN **101394-77-8** REGISTRY
CN 1,4-Butanediamine, N,N,N',N'-tetrakis(3-aminopropyl)-, hexahydrochloride (9CI) (CA INDEX NAME)
MF C16 H40 N6 . 6 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
CRN (120239-63-6)



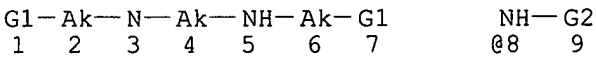
●6 HCl

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 131:228866

REFERENCE 2: 104:179019

=> d sta que l37
L30 SCR 1598
L31 SCR 1597 AND 1592
L32 SCR 1593
L34 STR



VAR G1=NH2/8
VAR G2=ME/ET/I-PR/N-PR
NODE ATTRIBUTES:
CONNECT IS M1 RC AT 3
CONNECT IS M1 RC AT 4
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M3 C AT 2
ECOUNT IS M3 C AT 6

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L37 943 SEA FILE=REGISTRY CSS FUL L34 AND (L30 OR L31) AND L32

100.0% PROCESSED 210556 ITERATIONS 943 ANSWERS
SEARCH TIME: 00.00.12

```
=> d sta que l85
L69             STR

 NH—G2       G1—G3—N—G3—G1       G1—G3—N—G3—G1
@8   9        1   2   3   4   5       14  13  12  11  10


VAR G1=NH2/8
VAR G2=ME/ET/I-PR/N-PR
REP G3=(3-4) C
NODE ATTRIBUTES:
CONNECT IS M3  RC AT   3
CONNECT IS M3  RC AT  12
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  12

STEREO ATTRIBUTES: NONE
L76             SCR 1598
L77             SCR 963 OR 1398
L79             SCR 1569
L82             SCR 1597
L83             SCR 1568
L85         142 SEA FILE=REGISTRY SSS FUL L69 AND (L79 OR (L83 AND L82 AND
                L77) OR (L76 AND L77))

100.0% PROCESSED 236943 ITERATIONS                          142 ANSWERS
SEARCH TIME: 00.00.10


=> d his

     (FILE 'HOME' ENTERED AT 08:08:40 ON 01 JUL 2002)
                SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 08:09:41 ON 01 JUL 2002
                E WO98-US7806/AP,PRN
L1            1 S E3,E4
                E POULIN R/AU
L2           60 S E3,E6
                E AUDETTE M/AU
L3           34 S E3,E4
                E CHAREST/AU
L4            6 S E21,E22
L5            1 S E55
                E GAUDREALT/AU
L6           25 S (POLYAMINE OR POLY AMINE) AND L2-L5
L7           19 S AMINE#/CW AND L2-L5
L8           25 S L6,L7
L9           14 S BIOLOGICAL TRANSPORT+NT/CT AND L8
                E BIOLOGICAL TRANSPORT/CT
                E E3+ALL
                E E60+ALL
L10           0 S E1+NT AND L8
L11          14 S L1,L9
L12          11 S L8 NOT L11
L13          24 S L11,L12 NOT L1
L14           1 S L8,L11,L12 NOT L13
                SEL RN
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     FILE 'REGISTRY' ENTERED AT 08:13:56 ON 01 JUL 2002
L15          34 S E1-E34
L16             STR
L17          50 S L16
L18             STR L16
L19           0 S L18
L20             STR L18
L21           0 S L20
L22             STR L20
L23           0 S L22
L24             SCR 2043
L25           0 S L22 NOT L24 SAM
L26             STR L18
L27           0 S L26
L28             STR L26
L29           0 S L28 CSS SAM
L30             SCR 1598
L31             SCR 1597 AND 1592
L32             SCR 1593
L33           2 S L28 AND (L30 OR L31) AND L32 CSS
L34             STR L18
L35           2 S L34 AND (L30 OR L31) AND L32 CSS SAM
L36           0 S L34 AND L32 CSS
L37         943 S L34 AND (L30 OR L31) AND L32 CSS FUL
                SAV L37 KUMAR529/A
L38             STR L34
L39           2 S L38 CSS SAM SUB=L37
L40           4 S L38 CSS FUL SUB=L37
                SAV L40 KUMAR529A/A
L41             STR L34
L42          32 S L41 CSS SAM SUB=L37
L43         752 S L41 CSS FUL SUB=L37
                SAV L43 KUMAR529B/A
L44             STR L41
L45           0 S L44 CSS SAM SUB=L43
L46          19 S L44 CSS FUL SUB=L43
                SAV L46 KUMAR529C/A
L47             STR L44
L48           0 S L47 CSS SAM SUB=L37
L49           2 S L47 CSS FUL SUB=L37
                SAV L49 KUMAR529D/A
L50             STR L47
L51           0 S L50 CSS SAM SUB=L37
L52           0 S L50 CSS FUL SUB=L37
                SAV L52 KUMAR529E/A
L53             STR
L54           2 S L53 SAM SUB=L37
L55           4 S L53 FUL SUB=L37
                SAV L55 KUMAR529F/A
L56          14 S L15 AND L37
L57           6 S L56 AND 10/N NOT C26H46N10O4S
L58          20 S L15 NOT L56
L59           2 S L58 AND (C20H40N6 OR C18H44N6S2)
L60           8 S L57,L59
L61             STR L34
L62           0 S L61 CSS
L63             STR L61
L64           0 S L63 CSS
L65             SCR 1996 AND 1593
L66           1 S L63 AND L65 CSS
L67             SCR 2043 OR 2039 OR 2050 OR 2049 OR 2053 OR 2052 OR 2051 OR 205
L68           0 S L63 AND L65 NOT L67 CSS
L69             STR L63
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L70           0 S L69 SAM
L71           0 S L69 AND L65 NOT L67 SAM
L72             SCR 2127
L73           0 S L69 AND L65 NOT (L67 OR L72) SAM
L74             SCR 1562
L75             SCR 1568 AND 1597
L76             SCR 1598
L77             SCR 963 OR 1398
L78           0 S L69 AND (L74 OR (L77 AND (L76 OR L75)))
L79             SCR 1569
L80           0 S L69 AND (L79 OR (L77 AND (L76 OR L75)))
L81             SCR 1595
L82             SCR 1597
L83             SCR 1568
L84           0 S L69 AND (L79 OR (L83 AND L82 AND L77) OR (L76 AND L77))
L85         142 S L69 AND (L79 OR (L83 AND L82 AND L77) OR (L76 AND L77)) FUL
                SAV L85 KUMAR529G/A
L86           9 S L69 CSS SAM SUB=L85
L87             SCR 2039 OR 2040
L88           0 S L69 NOT L87 CSS SAM SUB=L84
L89             SCR 2039
L90           9 S L69 NOT L89 CSS SAM SUB=L85
L91             SCR 2040
L92           6 S L69 NOT L91 CSS SAM SUB=L85
L93           3 S L90 NOT L92
L94         112 S L69 NOT L91 CSS FUL SUB=L85
                SAV L94 KUMAR529H/A
L95           4 S L53 FUL SUB=L94
                SAV L95 KUMAR529I/A
L96         108 S L94 NOT L95
L97           2 S L15 AND L85
L98           8 S L60,L97
L99          11 S L95,L98
L100        137 S L40,L46,L49,L95,L99,L60,L96

     FILE 'HCAPLUS' ENTERED AT 11:22:27 ON 01 JUL 2002
L101        193 S L100
L102          5 S L1-L5 AND L101
L103        120 S L101 AND (PY<=1998 OR PRY<=1998 OR AY<=1998)
L104         10 S L103 AND BIOLOGICAL TRANSPORT+NT/CT
                E BIOLOGICAL TRANSPORT+ALL/CT
                E E60+ALL
L105          0 S E1+NT AND L103
L106         64 S L103 AND (POLYAMINE OR POLY AMINE OR AMINE#/CW(L)POLY)
L107         10 S L106 AND TRANSPORT?
L108         82 S L100(L)(THU OR BAC OR BIOL OR USES)/RL
L109         58 S L108 AND L103
L110          9 S L109 AND L104
L111         11 S L109 AND TRANSPORT?
L112          0 S L109 AND SIGNAL?(L)TRANSDUC?
L113         15 S L102,L104,L110,L111
L114         13 S L113 NOT CDNA/TI
L115         10 S L103 AND 63/SC,SX
L116         15 S L114,L115
L117          5 S L116 AND TRANSPORT?(L)INHIBIT?
L118         10 S L106 AND L116
L119         15 S L116-L118
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 11:29:42 ON 01 JUL 2002
L120         37 S E1-E37

     FILE 'REGISTRY' ENTERED AT 11:30:47 ON 01 JUL 2002
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FILE 'HCAPLUS' ENTERED AT 11:31:47 ON 01 JUL 2002

FILE 'REGISTRY' ENTERED AT 11:32:35 ON 01 JUL 2002